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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	DEC 01	ChemPort single article sales feature unavailable
NEWS 3	APR 03	CAS coverage of exemplified prophetic substances enhanced
NEWS 4	APR 07	STN is raising the limits on saved answers
NEWS 5	APR 24	CA/CAplus now has more comprehensive patent assignee information
NEWS 6	APR 26	USPATFULL and USPAT2 enhanced with patent assignment/reassignment information
NEWS 7	APR 28	CAS patent authority coverage expanded
NEWS 8	APR 28	ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS 9	APR 28	Limits doubled for structure searching in CAS REGISTRY
NEWS 10	MAY 08	STN Express, Version 8.4, now available
NEWS 11	MAY 11	STN on the Web enhanced
NEWS 12	MAY 11	BEILSTEIN substance information now available on STN Easy
NEWS 13	MAY 14	DGENE, PCTGEN and USGENE enhanced with increased limits for exact sequence match searches and introduction of free HIT display format
NEWS 14	MAY 15	INPADOCDB and INPAFAMDB enhanced with Chinese legal status data
NEWS 15	MAY 28	CAS databases on STN enhanced with NANO super role in records back to 1992
NEWS 16	JUN 01	CAS REGISTRY Source of Registration (SR) searching enhanced on STN

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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                                                           ENTRY    SESSION
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DICTIONARY FILE UPDATES:  10 JUN 2009  HIGHEST RN 1155458-91-5

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experimental property data in the original document.  For information
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http://www.cas.org/support/stngen/stndoc/properties.html

=> e levosimendan
E1            1     LEVOSEMOTIADI/BI
E2            1     LEVOSEMOTIADIL/BI
E3            1 --> LEVOSIMENDAN/BI
E4            1     LEVOSIN/BI
E5            1     LEVOSINUM/BI
E6            1     LEVOSPASME/BI
E7            1     LEVOSTARCH/BI
E8            1     LEVOSULFIN/BI
E9            1     LEVOSULP/BI
E10           1     LEVOSULPIRID/BI
E11           1     LEVOSULPIRIDE/BI
E12           4     LEVOTAN/BI

=> s e3
L1            1 LEVOSIMENDAN/BI

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   141505-33-1  REGISTRY
ED   Entered STN:  22 May 1992
CN   Propanedinitrile, 2-[2-[4-[(4R)-1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl]phenyl]hydrazinylidene]-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Propanedinitrile, [[4-(1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl)phenyl]hydrazono]-, (R)-
CN   Propanedinitrile, [[4-[(4R)-1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl]phenyl]hydrazono]- (9CI)
OTHER NAMES:
CN   (-)-OR 1259
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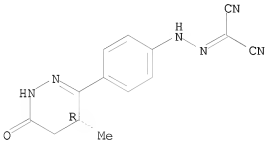
CN (R)-Simendan
CN Levosimendan
CN OR 1259
CN Simdax
FS STEREOSEARCH
MF C14 H12 N6 O
CI COM
SR World Health Organization (WHO)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

384 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
387 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

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FULL ESTIMATED COST	7.88	8.10

FILE 'CAPLUS' ENTERED AT 09:56:30 ON 12 JUN 2009
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FILE COVERS 1907 - 12 Jun 2009 VOL 150 ISS 25
FILE LAST UPDATED: 11 Jun 2009 (20090611/ED)

```
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Feb 2009

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> file caplus medline embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      0.50       8.60

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FILE 'MEDLINE' ENTERED AT 09:56:59 ON 12 JUN 2009

FILE 'EMBASE' ENTERED AT 09:56:59 ON 12 JUN 2009
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FILE 'BIOSIS' ENTERED AT 09:56:59 ON 12 JUN 2009
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=> s (l1 or levosimendan or simdax or simendan) and (renal or kidney) and
(insufficiency or failure)
L2          152 (L1 OR LEVOSIMENDAN OR SIMDAX OR SIMENDAN) AND (RENAL OR KIDNEY)
                AND (INSUFFICIENCY OR FAILURE)

=> s l2 and py<=2004
L3           35 L2 AND PY<=2004

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           29 DUP REM L3 (6 DUPLICATES REMOVED)

=> d l4 ibib abs 1-29

L4   ANSWER 1 OF 29  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2006:891335  CAPLUS
DOCUMENT NUMBER:          145:263302
TITLE:                    Methods of cardioprotection using dichloroacetate in
                          combination with an inotrope
INVENTOR(S):              Lopaschuk, Gary D.; Collins-Nakai, Ruth
PATENT ASSIGNEE(S):       University of Alberta, Can.
SOURCE:                   U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S.
                          Ser. No. 13,666.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   5
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------------    ----   --------    --------------------   --------
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US 20060194878 A1 20060831 US 2005-229101 20050916
US 6693133 B1 20040217 US 2002-268069 20021007 <--
US 20040162346 A1 20040819 US 2004-778791 20040213 <--
US 7432247 B2 20081007
US 20050282896 A1 20051222 US 2004-13666 20041215
WO 2006063446 A1 20060622 WO 2005-CA1894 20051215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
WO 2007030944 A2 20070322 WO 2006-CA1523 20060915
WO 2007030944 A3 20070503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2002-268069 A1 20021007
US 2004-778791 A2 20040213
US 2004-13666 A2 20041215
US 2005-229101 A 20050916

AB The invention provides methods for maintaining or improving cardiac function after a cardiac function disturbing event by the use of cardioprotective dichloroacetate (DCA) and a inotropic drug. The invention also provides pharmaceutical compns. comprising the combination of DCA and inotropic drug, pharmaceutically acceptable carriers and optional other therapeutic agents. Also provided are the dosage protocols for the DCA and inotropic drug combination.

L4 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:589420 CAPLUS
DOCUMENT NUMBER: 141:82329
TITLE: levosimendan and active metabolite for treatment of renal failure in mammals
INVENTOR(S): Kivikko, Matti; Haikala, Heimo
PATENT ASSIGNEE(S): Orion Corporation, Finland
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060375	A1	20040722	WO 2004-FI2	20040102 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ

CA 2511735	A1	20040722	CA 2004-2511735		20040102 <--
EP 1581227	A1	20051005	EP 2004-700048		20040102
EP 1581227	B1	20070228			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

AT 355063	T	20060315	AT 2004-700048		20040102
JP 2006515348	T	20060525	JP 2006-500147		20040102
ES 2281775	T3	20071001	ES 2004-700048		20040102
US 20060166994	A1	20060727	US 2006-541394		20060329
PRIORITY APPLN. INFO.:			FI 2003-15	A	20030103
			WO 2004-FI2	W	20040102

AB Levosimendan or its active metabolite are useful in reducing mortality in mammals suffering from renal failure.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 29 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER:	2005065095 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 15693696
TITLE:	Levosimendan in daily intensive care practice--the experience of 15 centers. Background, methods and organization of the PORTLAND study.
AUTHOR:	Cardoso J Silva; Ferreira Jorge; de Sa Edwiges Prazeres; de Campos J Martins; Fonseca Candida; Lousada Nuno; Moreira J Ilidio; Rabacal Carlos; Damasceno Albertino; Seabra-Gomes Ricardo; Ferreira Rafael; Abreu e Lima Cassianosilvacardoso30@hotmail.com
SOURCE:	Revista portuguesa de cardiologia : orgao oficial da Sociedade Portuguesa de Cardiologia = Portuguese journal of cardiology : an official journal of the Portuguese Society of Cardiology, (2004 Nov) Vol. 23, No. 11, pp. 1431-43. Journal code: 8710716. ISSN: 0870-2551.
PUB. COUNTRY:	Portugal
DOCUMENT TYPE:	(CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY)
LANGUAGE:	English; Portuguese
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200503
ENTRY DATE:	Entered STN: 8 Feb 2005 Last Updated on STN: 18 Mar 2005 Entered Medline: 17 Mar 2005

AB INTRODUCTION: The LIDO and RUSSLAN trials showed that levosimendan was well tolerated and had a stronger hemodynamic effect than dobutamine and a positive impact on prognosis. There are, however, few data regarding its effectiveness and safety when used in an everyday clinical setting. OBJECTIVE: To test the hypothesis that in day-to-day practice conditions levosimendan is both effective and safe for the treatment of decompensated heart failure (HF). This primary combined endpoint of effectiveness and safety was evaluated at 24 hours and 5 days after the beginning of the treatment. DESIGN: Prospective, multicenter, nonrandomized clinical trial with evaluations at baseline, 24 hours, 5 days, and 3 and 6 months. Follow-up for 6 months. SETTING: The intensive care units of 15 cardiology or internal medicine departments. PATIENTS: 129 consecutive patients requiring inotropes due to decompensated systolic HF despite maximally tolerated oral therapy. Intervention: 24-hour infusion of levosimendan via a central or

peripheral vein. MEASUREMENTS AND EVALUATION OF RESULTS: 1. Monitoring: Continuous ECG monitoring, non-invasive blood pressure, urinary output, oximetry. Invasive monitoring was not required. 2. Follow-up. Baseline evaluation: history, physical examination, ECG, 2D echocardiogram, hemogram, ionogram, liver and kidney function. 24-hour and 5-day evaluations: symptoms, physical examination, recording of medical therapy and previous 24-hour urinary output, ECG, hemogram, ionogram, liver and kidney function, and evaluation of arrhythmic episodes and heart rate and blood pressure trends in previous 24 hours. 3- and 6-month evaluations: number of hospital admissions and length of hospital stay due to HF, and mortality. 3. Evaluation of primary endpoint. EFFECTIVENESS: assessed by a clinical score including 2 subjective parameters (1. NYHA functional class, 2. patient self-evaluation symptom class) and 6 objective parameters (3. body weight, 4. pulmonary congestion, 5. previous 24-hour diuresis, 6. serum creatinine, 7. oral HF medication, 8. intravenous HF medication). Definition of clinical effectiveness: improvement in > or = 1 subjective parameters plus improvement in > or = 1 objective parameters, with all other parameters unchanged. Safety: The therapy was judged safe in the absence of any serious adverse event with a probable or undetermined causal relationship with levosimendan. Primary endpoint evaluation: Patients reached the primary endpoint when levosimendan was both effective and safe according to the above definitions.

L4 ANSWER 4 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004346409 EMBASE
TITLE: Clinical trials update from the European Society of Cardiology Heart Failure meeting: SHAPE, BRING-UP 2 VAS, COLA II, FOSIDIAL, BETACAR, CASINO and meta-analysis of cardiac resynchronisation therapy.
AUTHOR: Coletta, Alison P. (correspondence); Cleland, John G.F.; Clark, Andrew L.
CORPORATE SOURCE: Department of Academic Cardiology, University of Hull, Castle Hill Hosp., Cottingham, H., Kingston-upon-Hull, United Kingdom. a.p.coletta@hull.ac.uk
AUTHOR: Freemantle, Nick
CORPORATE SOURCE: Dept. of Prim. Care and Gen. Pract., University of Birmingham, Edgbaston, B15 2TT, Birmingham, United Kingdom.
SOURCE: European Journal of Heart Failure, (Aug 2004) Vol. 6, No. 5, pp. 673-676.
Refs: 6
ISSN: 1388-9842 CODEN: EJHFFS
PUBLISHER IDENT.: S 1388-9842(04)00209-0
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Sep 2004
Last Updated on STN: 2 Sep 2004

AB This article continues a series of reports on recent research developments in the field of heart failure. Key presentations made at the European Society of Cardiology Heart Failure Update meeting, held in Wroclaw, Poland, in June 2004 are reported. The SHAPE study identified a need to educate general practitioners (GPs) in order to optimise treatment of heart failure in primary care. BRING-UP 2 VAS showed that cognitive impairment is very common in elderly heart failure patients and that these patients require specialist care.

Carvedilol was shown to be well tolerated and effective in elderly heart failure patients in the observational COLA II study. In the FOSIDIAL study of patients with end-stage renal disease, fosinopril showed no benefit over placebo in reducing the incidence of cardiovascular events in these high-risk patients. The BETACAR study showed that carvedilol and metoprolol produced a similar effect on left ventricular ejection fraction (+13.1% and +12.0%, respectively). Revised mortality data for the CASINO study and a meta-analysis of the effects of cardiac resynchronisation therapy on mortality in the light of the recently published COMPANION study are reported.

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ACCESSION NUMBER: 2004263690 EMBASE
TITLE: [Diagnostic and therapeutic progress: Venous thromboembolism, heart failure and radio contrast agents].
Progres diagnostiques et therapeutiques: Maladie veineuse thrombo-embolique, insuffisance cardiaque, produits de contraste.
AUTHOR: Genest, Marc (correspondence)
CORPORATE SOURCE: Service de Cardiologie, CH Provins, BP 212, 77488 Provins Cedex, France. marc.genest@wanadoo.fr
AUTHOR: Pochmalicki, Gilbert
SOURCE: Presse Medicale, (22 May 2004) Vol. 33, No. 9 I, pp. 623-629.
Refs: 28
ISSN: 0755-4982 CODEN: PRMEEM
COUNTRY: France
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 014 Radiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 15 Jul 2004
Last Updated on STN: 15 Jul 2004

AB Modalities for the diagnosis of venous thromboembolism Currently rely on the confrontation of the initial clinical data and the results of D-dimer measurements, a venous Doppler, although reliable, is not a first-line exploration. Regarding treatment Indications for thrombolysis are currently limited to massive pulmonary oedema with shock. Alteplase added to heparin improves the progression of severe embolism; it spares the patients from heavy interventions of resuscitation but the mortality remains the same. Concerning anticoagulant treatments, prolonged antivitamin K at classical doses is more effective than low dosesand for limited duration if phlebitis is an idiopathic one. For heart failure with preserved ejection fraction Treatment of these heart failures, formerly know as 'diastolic' is similar to that of the acute phase of systolic heart failure. However, care should be taken with vasodilatators. Concerning heart failure in general The brain natriuretic peptide (BNP) represents a remarkable progress for the aetiological diagnosis of dyspnoea (inferior to 80 pg/ml in the case of pulmonary origin, superior to 300 pg/ml in the case of cardiac origin or severe pulmonary embolism). Regarding treatment, for acute heart failure, it is still the association of nitrates and diuretics, with oxygen therapy and eventually inotropics. Beta-blockers, which have revolutionized the treatment of chronic heart failure, must be maintained whenever possible in the case of the onset of acute pulmonary oedema. Multisite pacing is increasingly used in refractory chronic heart

failure. Implantable defibrillation has become common practice. Non-invasive ventilation (Bi or C-PAP) is interesting in acute cardiogenic pulmonary oedema. The preventive role of N acetyl-cysteine N acetyl cysteine reduces the incidence of nephropathies induced by the radio contrast products in patients with chronic kidney failure. Combined with hydratation, it must be proposed the day before and on the day of the procedure in any patient with diabetes or kidney failure.

L4 ANSWER 6 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:345753 BIOSIS
DOCUMENT NUMBER: PREV200510136493
TITLE: A new method for the assessment of myocardial viability and prediction of the result of revascularization.
AUTHOR(S): Pavlakis, G. [Reprint Author]; Bouki, K.; Komninos, K.; Kostopoulos, K.; Foulidis, V.; Kakavas, T.; Xydas, T.; Papasteriadis, E.
CORPORATE SOURCE: Gen Hosp Nikea, Cardiol Dept 1, Piraeus, Greece
SOURCE: European Heart Journal, (AUG-SEP 2004) Vol. 25, No. Suppl. S, pp. 553-554.
Meeting Info.: ESC Congress 2004. Munich, GERMANY. August 28 -September 01, 2004. ESC.
CODEN: EHJODF. ISSN: 0195-668X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Sep 2005
Last Updated on STN: 8 Sep 2005

L4 ANSWER 7 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004133436 EMBASE
TITLE: [What is the relevance of anemia treatment among the novel therapies of heart failure?].
Que lugar ocupa el tratamiento de la anemia en la insuficiencia cardiaca?.
AUTHOR: Carnevali Ruiz, Daniel, Dr. (correspondence)
CORPORATE SOURCE: Area de Medicina Interna, Clinica Moncloa (ASISA), Avda. de Valladolid, 83, 28008 Madrid, Spain.
SOURCE: Medicina Clinica, (7 Feb 2004) Vol. 122, No. 4, pp. 136-137.
Refs: 11
ISSN: 0025-7753 CODEN: MCLBA2
COUNTRY: Spain
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
006 Internal Medicine
LANGUAGE: Spanish; Castilian
ENTRY DATE: Entered STN: 12 Apr 2004
Last Updated on STN: 12 Apr 2004

L4 ANSWER 8 OF 29 MEDLINE on STN
ACCESSION NUMBER: 2006173222 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16566697
TITLE: Levosimendan following coronary artery bypass grafting in a patient with end-stage renal failure: a case report.
AUTHOR: Raftopoulos S C
CORPORATE SOURCE: Department of Intensive Care Medicine, Sir Charles Gairdner Hospital, Nedlands, Western Australia..
spiro@graduate.uwa.edu.au

SOURCE: Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine, (2004 Jun) Vol. 6, No. 2, pp. 109-12. Journal code: 100888170. ISSN: 1441-2772.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; PUBMED-NOT-MEDLINE
ENTRY MONTH: 200604
ENTRY DATE: Entered STN: 29 Mar 2006
Last Updated on STN: 22 Apr 2006
Entered Medline: 21 Apr 2006

AB Levosimendan is a novel inotropic agent indicated for patients with decompensated heart failure. It has well recognised mechanisms of action. Its use however, has not been described in patients with end-stage renal failure. This report describes the use of levosimendan in a post-operative coronary artery bypass graft patient with decompensated heart failure and end-stage renal failure previously receiving dialysis six days per week. Levosimendan proved to be a safe and useful agent when used as a continuous intravenous infusion initially at 0.05 microg/kg/min then increasing up to 0.2 microg/kg/min for a total of 42 hours.

L4 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:51937 CAPLUS
DOCUMENT NUMBER: 140:350704
TITLE: Vasoactive drugs and the kidney
AUTHOR(S): Lee, Raymond Wai Chuen; Di Giantomasso, David; May, Clive; Bellomo, Rinaldo
CORPORATE SOURCE: Department of Intensive Care and Department of Medicine, Florey Institute of Physiology, Austin Hospital, Melbourne, Australia
SOURCE: Best Practice & Research, Clinical Anaesthesiology (2004), 18(1), 53-74
CODEN: BPRCD8
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Protection of renal function and prevention of acute renal failure (ARF) are important goals of resuscitation in critically ill patients. Beyond fluid resuscitation and avoidance of nephrotoxins, little is known about how such prevention can be achieved. Vasoactive drugs are often administered to improve either cardiac output or mean arterial pressure in the hope that renal blood flow will also be improved and, thereby, renal protection achieved. Some of these drugs (especially low-dose dopamine) have even been proposed to have a specific beneficial effect on renal blood flow. However, when all studies dealing with vasoactive drugs and their effects on the kidney are reviewed, it is clear that none were demonstrated to achieve clin. important benefits in terms of renal protection. It is also clear that, with the exception of low-dose dopamine, there were no randomized controlled trials of sufficient statistical power to detect differences in clin. meaningful outcomes. In the absence of such data, all that is available is based on limited physiol. gains (changes in renal blood flow or urine output) with one or another drug in one or another subpopulation of patients. Furthermore, given the authors' lack of understanding of the pathogenesis of ARF, it is unclear whether hemodynamic manipulation is an appropriate avenue to achieve renal protection. There is a great need for large randomized controlled trials to test the clin., instead of physiol., effects of vasoactive drugs in critical illness.

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2004390616 EMBASE
TITLE: New pharmacological treatments of acutely decompensated heart failure. Critical review of new drug options.
AUTHOR: Naccarella, Franco, Dr. (correspondence); Lepera, Giovannina; Gatti, Mauro; Pazzaglia, Stefano; Spinelli, Giovanna; Bresciani, Barbara
CORPORATE SOURCE: Cardiology Department, Day Hospital Tiarini Corticella, Azienda USL Citta di Bologna, Bologna, Italy.
AUTHOR: Naccarelli, Gerald
CORPORATE SOURCE: Cardiology Department, Penn State University, Hershey, PA, United States.
AUTHOR: Liying, Chen; Ambrosioni, Ettore; Borghi, Claudio
CORPORATE SOURCE: Clinica Medica III, University of Bologna, Bologna, Italy.
AUTHOR: Maranga, Stefano Sdringola
CORPORATE SOURCE: Cardiology Department, Hermann Hospital, Houston, TX, United States.
AUTHOR: Arpesella, Giorgio
CORPORATE SOURCE: Cardiosurgical Department, University of Bologna, Bologna, Italy.
AUTHOR: Liying, Chen; Ambrosioni, Ettore; Borghi, Claudio
CORPORATE SOURCE: Cardiology Department, Anzhen Hospital, Pijing, China.
AUTHOR: Naccarella, Franco, Dr. (correspondence)
CORPORATE SOURCE: Via Mascarella 77/5, 40126 Bologna, Italy.
AUTHOR: Naccarella, Franco, Dr. (correspondence)
CORPORATE SOURCE: Via Mascarella 77/5, 40126 Bologna, Italy.
SOURCE: Mediterranean Journal of Pacing and Electrophysiology, (Jan 2004) Vol. 6, No. 1, pp. 7-24.
Refs: 145
ISSN: 1128-4293 CODEN: MJPEAC
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Sep 2004
Last Updated on STN: 30 Sep 2004

AB Acutely decompensated heart failure (ADHF) represents the leading reason for hospital admissions in patients over 65 years of age. Aim of this paper is to analyze new approaches for acute heart failure treatment. Effective new treatments should be found to reduce the length of hospital stay and its correlate costs in CHF symptomatic and asymptomatic patients. According to the Authors' personal experience and new clinical data from controlled clinical trials, it is mandatory to substitute traditional inotropes, in acutely decompensated heart failure, as first option, with the advice to use alternative drugs, at least in patients with the cardio renal syndrome. The Author consider the possibility of treatment of ADHF trying toblock mainly compensatory systems and neurohermons.

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ACCESSION NUMBER: 2005005514 EMBASE

TITLE: Clinical decision making in managing the 'difficult' patient with chronic heart failure: Who, when, how, where?.
AUTHOR: Krum, H.
CORPORATE SOURCE: NHMRC Ctr. Clin. Res. Excellence T., Depts. Epidemiology AndPreventive M., Monash Univ. Ctrl. E. Clin. Sch., A..
AUTHOR: Krum, H.
CORPORATE SOURCE: NHMRC Ctr. Clin. Res. Excellence T., Depts. Epidemiol. Prev. Med. Med., Monash Univ. Ctrl. E. Clin. Sch., A..
SOURCE: European Heart Journal, Supplement, (Dec 2004) Vol. 6, No. 9, pp. I88-I96.
Refs: 58
ISSN: 1520-765X CODEN: EHJSFT
PUBLISHER IDENT.: S 1520-765X(03)80014-7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jan 2005
Last Updated on STN: 20 Jan 2005

AB Chronic heart failure (CHF) is a complex disorder, and all patients with this condition could therefore be considered 'difficult'. Nevertheless, there are certain subgroups in whom management poses greater challenges. These include patients with advanced disease severity, complications arising from CHF, comorbidities, and patients in whom it is difficult to optimize standard therapies. Advanced disease is associated with reduced quality of life, frequent hospitalization and poor survival Major challenges in advanced CHF include ensuring adequate tolerability of therapy, keeping patients out of hospital and decision making regarding palliation. Complications such as tachyarrhythmias and bradyarrhythmias may also alter management. CHF is a pro-thromboembolic state, but the role of anticoagulation and antiplatelet therapy is unclear. Weight loss is an independent prognostic marker for poor survival in complicated CHF, and therapies directed at reducing weight loss may improve outcome. Comorbid conditions that may affect decision making in the patient with CHF include aetiological contributors (e.g. ischaemic heart disease, hypertension, diabetes mellitus and anaemia) and other comorbid disorders such as respiratory disease, cognitive dysfunction, depression, renal failure and arthritis. In some clinical scenarios, optimal therapy may not easily be achieved. In patients with low systemic blood pressure, vasodilating drugs may be difficult to use. Bradyarrhythmias or bronchial hyperreactivity may limit the use of beta-blockers. Drug therapy may also be difficult to optimize in patients with advanced renal dysfunction. .COPYRGT. 2003 The European Society of Cardiology. Published by Elsevier Science Ltd.

L4 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:319257 CAPLUS
DOCUMENT NUMBER: 138:343856
TITLE: Buccal sprays or capsules containing cardiovascular or renal drugs
INVENTOR(S): Dugger, Harry A., III
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 537,118.
CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030077229	A1	20030424	US 2002-230075	20020829 <--
WO 9916417	A1	19990408	WO 1997-US17899	19971001 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 1036561	A1	20000920	EP 2000-109357	19971001 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1952802	A2	20080806	EP 2007-23005	19971001
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
EP 2042161	A1	20090401	EP 2008-20267	19971001
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2496769	A1	20040311	CA 2003-2496769	20030827 <--
WO 2004019909	A2	20040311	WO 2003-US26853	20030827 <--
WO 2004019909	A3	20040708		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003270014	A1	20040319	AU 2003-270014	20030827 <--
EP 1536769	A2	20050608	EP 2003-751909	20030827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006502147	T	20060119	JP 2004-531569	20030827
US 20050025713	A1	20050203	US 2004-928979	20040827
US 20080170995	A1	20080717	US 2007-929368	20071030
JP 2009079060	A	20090416	JP 2008-266598	20081015
US 20090123387	A1	20090514	US 2009-351490	20090109

PRIORITY APPLN. INFO.:

WO 1997-US17899	A2	19971001
US 2000-537118	A2	20000329
EP 1997-911621	A3	19971001
JP 2000-513555	A3	19971001
US 2002-230075	A	20020829
WO 2003-US26853	W	20030827

AB Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation A: aqueous polar solvent, active compound, and optional flavoring agent; formulation B: aqueous polar solvent, active compound, optionally flavoring agent, and propellant; formulation C: non-polar solvent, active compound, and optional flavoring agent; and formulation D: non-polar solvent, active compound, optional flavoring agent, and propellant. Thus, a polar lingual spray contained

isoproterenol-HCl 0.5-6, water 50-75, EtOH 5-10, PEG 5-15, sorbitol 0.4-1.0, aspartame 0.04-0.1, and flavors 2-3%.

L4 ANSWER 13 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:35535 BIOSIS
DOCUMENT NUMBER: PREV200400033329
TITLE: Prognostic markers of levosimendan treatment efficacy in severe congestive heart failure: A prospective multicentre Study.
AUTHOR(S): Bocchi, E. [Reprint Author]; Guimaraes, G. [Reprint Author]; Vilas-Boas, F.
CORPORATE SOURCE: Medical School, Heart Institute (InCor), University of Sao Paulo, Sao Paulo, Brazil
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print. Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology. ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L4 ANSWER 14 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:35534 BIOSIS
DOCUMENT NUMBER: PREV200400033328
TITLE: Levosimendan is efficacious in acute heart failure independent of renal function.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author]; Providencia, L. A. [Reprint Author]
CORPORATE SOURCE: Cardiology Dept., Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print. Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology. ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L4 ANSWER 15 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:35533 BIOSIS
DOCUMENT NUMBER: PREV200400033327
TITLE: Levosimendan is beneficial in diabetics with acute heart failure.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author];

Providencia, L. [Reprint Author]
CORPORATE SOURCE: Cardiology Department, Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 407. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L4 ANSWER 16 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003301348 EMBASE
TITLE: Clinical use of inotropic therapy for heart failure : Looking backward or forward? Part I: Inotropic infusions during hospitalization.
AUTHOR: Stevenson, Lynne Warner, Dr. (correspondence)
CORPORATE SOURCE: Division of Cardiology, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115, United States.
SOURCE: Circulation, (22 Jul 2003) Vol. 108, No. 3, pp. 367-372. Refs: 50
ISSN: 0009-7322 CODEN: CIRCAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Aug 2003
Last Updated on STN: 14 Aug 2003

L4 ANSWER 17 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003256920 EMBASE
TITLE: Gateways to clinical trials: May 2003.
AUTHOR: Bayes, M. (correspondence)
CORPORATE SOURCE: Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
AUTHOR: Rabasseda, X.; Prous, J.R.
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (May 2003) Vol. 25, No. 4, pp. 317-340. Refs: 143
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2003
Last Updated on STN: 17 Jul 2003
AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity®, the drug discovery and development portal,

http://integrity.prous.com. This issue focuses on the following selection of drugs: 2F5, 2G12, Abetimus sodium, ABI-007, adalimumab, adefovir dipivoxil, AE-941, alefacept, altropane, aminolevulinic acid hydrochloride, aminolevulinic acid methyl ester, aminopterin, anakinra, aprinocarsen sodium, atazanavir, atlizumab, atomoxetine hydrochloride; B7-1 vaccine, bevacizumab, biricodar dicitrate, BMS-188667, brasofensine sulfate, bryostatin 1; Cantuzumab mertansine, CHS-828, cinacalcet hydrochloride, cipamfylline, creatine, CVT-3146; Darbepoetin alfa, DITPA, drotrecogin alfa (activated), duloxetine hydrochloride; Edatrexate, efalizumab, ENMD-0997, epoetin, erlosamide, esomeprazole magnesium, etiprednol dicloacetate, etoricoxib, everolimus, ezetimibe; Fampridine, fenretinide, FTY-720; IGF-I/IGFBP-3 IL-1 cytokine trap, ilodecakin, interferon beta, ISIS-104838, ISIS-2503, ISIS-5132, ivabradine hydrochloride; Lafutidine, lanthanum carbonate, L-Arginine hydrochloride, LEA29Y, lerdelimumab, levetiracetam, levobupivacaine hydrochloride, levosimendan, lopinavir; Melagatran, mibefradil hydrochloride, miglustat, morphine-6-glucuronide; Nesiritide; Omalizumab, omapatrilat; p24-VLP, parecoxib sodium, peginterferon alfa-2a, peginterferon alfa-2b, pegsunercept, pitavastatin calcium, plevitrexed, prasterone, pregabalin, PRO-2000, prucalopride; Rapacuronium bromide, rebimastat, RGA-0853, rubitecan, ruboxistaurin mesilate hydrate, RWJ-67657; S-16020-2, sarizotan, SLV-306, stiripentol; TA-CIN, tenecteplase, teriparatide, tezacitabine, tipifarnib, trabectedin, troglitazone; Valdecoxib, vardenafil; Z-338, ziconotide. .COPYRGT. 2003 Prous Science. All rights reserved.

L4 ANSWER 18 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:	2003156768 EMBASE
TITLE:	Projecting future drug expenditures - 2003.
AUTHOR:	Shah, Nilay D.; Vermeulen, Lee C. (correspondence)
CORPORATE SOURCE:	Center for Drug Policy, Univ. of Wisconsin Hosp. and Clinics, 600 Highland Avenue, Madison, WI 53792, United States.
AUTHOR:	Shah, Nilay D.
CORPORATE SOURCE:	Dept. of Population Health Sciences, School of Medicine, Univ. Wisconsin-Madison (UW-Madison), Madison, WI, United States.
AUTHOR:	Hoffman, James M.
CORPORATE SOURCE:	Outcomes Res./Medication Use Policy, UWHC, Madison, WI, United States.
AUTHOR:	Vermeulen, Lee C. (correspondence)
CORPORATE SOURCE:	School of Pharmacy, UW-Madison, Madison, WI, United States.
AUTHOR:	Hunkler, Robert J.; Hontz, Karrie M.
CORPORATE SOURCE:	Business Development, IMS HEALTH, Plymouth Meeting, PA, United States.
SOURCE:	American Journal of Health-System Pharmacy, (15 Jan 2003) Vol. 60, No. 2, pp. 137-149. Refs: 46 ISSN: 1079-2082 CODEN: AHSPEK
COUNTRY:	United States
DOCUMENT TYPE:	Journal; General Review; (Review)
FILE SEGMENT:	017 Public Health, Social Medicine and Epidemiology 036 Health Policy, Economics and Management 037 Drug Literature Index
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 1 May 2003 Last Updated on STN: 1 May 2003

AB Drug expenditure projections for 2003 and factors likely to influence drug costs are discussed. The United States continues to face the challenge of increased growth in health expenditures, and drug expenditures are

continuing to increase faster than the growth in total health care expenditures. These increases can be largely attributed to an increase in the average age of the U.S. population and technological advancement. On the basis of price inflation and non-price inflationary factors, including increases in volume, shifts in patient and therapeutic intensity, and expected approval of new drugs, a 10-12% increase in drug expenditures in 2003 for the inpatient setting and a 13.5-15.5% increase for ambulatory care settings are forecasted. While few new drugs are expected to greatly influence expenditures in 2003, the continued diffusion of recently approved drugs such as drotrecogin alfa and nesiritide will have a dramatic impact on total drug expenditures and must be carefully considered in the budgeting process. An agent likely to have a significant impact on HIV treatment is enfuvirtide, the first in a new class of antiretrovirals (fusion inhibitors), but its high cost ($10,000-$15,000 per year) may limit patients' access to this medication. An expanded user's guide is provided to assist the reader in appropriate application of this information in the drug budgeting process. Technological, demographic, and market-based changes and changes in public policy will continue to influence pharmaceutical expenditures in the coming year. An understanding of the overall drivers of medication expenditures and vigilance in monitoring pharmaceutical innovation are critical in the effective management of these resources.

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ACCESSION NUMBER: 2003158036 EMBASE
TITLE: [Cardiac failure in intensive care].
Srdecni selhani v intenzivni peci.
AUTHOR: Parizkova, R., Dr. (correspondence)
CORPORATE SOURCE: Univerzita Karlova v Praze, Lekarska Fakulta v Hradci Kralove, Fakultni Nemocnice Hradec Kralove, 500 05 Hradec Kralove, Czech Republic.
AUTHOR: Parizkova, R., Dr. (correspondence)
CORPORATE SOURCE: Klin. Anesteziol. Resuscitace/I. M., Fakultni Nemocnice, 500 05 Hradec Kralove, Czech Republic.
SOURCE: Anesteziologie a Neodkladna Pece, (2003) Vol. 14, No. 2, pp. 103-110.
Refs: 27
ISSN: 0862-4968 CODEN: ANPEFF
COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
024 Anesthesiology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Czech
SUMMARY LANGUAGE: English; Czech
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 1 May 2003

AB Heart failure represents almost 5 % of all hospital admissions and both mortality and health care cost on account of those patients are high. The proportion of patients on ICU with heart failure of various origin (mostly as a results either of primary heart damage or as a result of secondary heart damage due to multiple organ failure) has increased rapidly during the last two decades. Heart failure occurs mostly as a result of ischaemic heart disease and the prevalence of heart failure increases in those with both ischaemic heart disease and hypertension. Increased sympathetic activity, renin-angiotensin-aldosterone axis, vasopressin, endothelin and atrial natriuretic peptides play the most important role in developing heart failure. Current definitions, diagnosis and recommended treatment

of heart failure are based on recommendation issued by European Society of Cardiology. Echocardiography together with assessment of atrial natriuretic peptide plasma levels are preferred methods for diagnosis. The current therapeutic approach to heart failure is stratified according to levels of evidence based medicine methodology. The control of underlying cause and optimizing of myocardial oxygen delivery to failing heart without increasing oxygen consumption at the same time represent the cornerstone of therapy in heart failure patients. Diuretics, vasodilators together with inotropic agents (dobutamine, phosphodiesterase inhibitors and recently calcium sensitizers, if necessary), are the most recommended drugs in this setting. ACE inhibitors and beta-blockers are the key agents for long-term pharmacological therapy in chronic heart failure patients. Non-pharmacological modalities are also mentioned.

L4 ANSWER 20 OF 29 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003105353 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12617746
TITLE: 15th Annual Congress of the European Society of Intensive Care Medicine, 29 September-2 October 2002, Barcelona, Spain: clinical research to improve outcome.
AUTHOR: Dubois Marc-Jacques; Verdant Colin L; Bouali Redouane
CORPORATE SOURCE: Intensivist, Critical Care Medicine Division, University of Montreal Hospital, Montreal, Quebec, Canada.. marc-jacques.dubois@umontreal.ca
SOURCE: Critical care (London, England), (2003 Feb) Vol. 7, No. 1, pp. 91-4. Electronic Publication: 2003-01-06. Journal code: 9801902. ISSN: 1364-8535. Report No.: NLM-PMC154115.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Conference; Conference Article; (CONGRESSES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 6 Mar 2003
Last Updated on STN: 3 May 2003
Entered Medline: 2 May 2003

L4 ANSWER 21 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:15784 BIOSIS
DOCUMENT NUMBER: PREV200400013587
TITLE: Development of a comprehensive new endpoint for the evaluation of new treatments for acute decompensated heart failure: Results with levosimendan in the REVIVE-1 Study.
AUTHOR(S): Packer, M. [Reprint Author]; Colucci, W. S.; Fisher, L.; Massie, B. M.; Teerlink, J. R.; Young, J. B.; Garratt, C.
CORPORATE SOURCE: Medicine, Columbia University, New York, NY, USA
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 24. print. Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology. ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

L4 ANSWER 22 OF 29 MEDLINE on STN

ACCESSION NUMBER: 2003084974 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12594447
TITLE: Current medical treatment for the exacerbation of chronic heart failure resulting in hospitalization.
AUTHOR: Jain Parag; Massie Barry M; Gattis Wendy A; Klein Livin; Gheorghiade Mihai
CORPORATE SOURCE: Northwestern University, Feinberg School of Medicine, Chicago, Ill 60611, USA.
SOURCE: American heart journal, (2003 Feb) Vol. 145, No. 2 Suppl, pp. S3-17. Ref: 68
Journal code: 0370465. E-ISSN: 1097-6744.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 25 Feb 2003
Last Updated on STN: 13 Mar 2003
Entered Medline: 12 Mar 2003

L4 ANSWER 23 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003494488 EMBASE
TITLE: Clinical decision making in managing the 'difficult' patient with chronic heart failure: Who, when, how, where?.
AUTHOR: Krum, Henry, Prof. (correspondence)
CORPORATE SOURCE: Dept. of Epidemiol. and Prev. Med., Monash Univ. Ctrl. and E. Clin. Sch., Alfred Hospital, Melbourne, Vic. 3004, Australia.
SOURCE: European Heart Journal, Supplement, (Dec 2003) Vol. 5, No. I, pp. I88-I96.
Refs: 58
ISSN: 1520-765X CODEN: EHJSFT
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Dec 2003
Last Updated on STN: 30 Dec 2003

AB Chronic heart failure (CHF) is a complex disorder, and all patients with this condition could therefore be considered 'difficult'. Nevertheless, there are certain subgroups in whom management poses greater challenges. These include patients with advanced disease severity, complications arising from CHF, comorbidities, and patients in whom it is difficult to optimize standard therapies. Advanced disease is associated with reduced quality of life, frequent hospitalization and poor survival. Major challenges in advanced CHF include ensuring adequate tolerability of therapy, keeping patients out of hospital and decision making regarding palliation. Complications such as tachyarrhythmias and bradyarrhythmias may also alter management. CHF is a pro-thromboembolic state, but the role of anticoagulation and antiplatelet therapy is unclear. Weight loss is an independent prognostic marker for poor survival in complicated CHF, and therapies directed at reducing weight loss may improve outcome. Comorbid conditions that may affect decision making in the patient with CHF include aetiological contributors (e.g. ischaemic heart disease, hypertension, diabetes mellitus and anaemia) and other comorbid disorders

such as respiratory disease, cognitive dysfunction, depression, renal failure and arthritis. In some clinical scenarios, optimal therapy may not easily be achieved. In patients with low systemic blood pressure, vasodilating drugs may be difficult to use. Bradyarrhythmias or bronchial hyperreactivity may limit the use of beta-blockers. Drug therapy may also be difficult to optimize in patients with advanced renal dysfunction.

L4 ANSWER 24 OF 29 EMBASE

ACCESSION NUMBER: 2002164027 EMBASE
TITLE: New therapeutic options in congestive heart failure : Part I.
AUTHOR: McMurray, John, Dr. (correspondence); Pfeffer, Marc A.
CORPORATE SOURCE: Clin. Res. Initiative Heart Failure, University of Glasgow, Wolfson Building, Glasgow G12 8QQ, United Kingdom.
SOURCE: Circulation, (30 Apr 2002) Vol. 105, No. 17, pp. 2099-2106. Refs: 72
ISSN: 0009-7322 CODEN: CIRCAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002

L4 ANSWER 25 OF 29 EMBASE

ACCESSION NUMBER: 2002247703 EMBASE
TITLE: Present and future pharmacotherapy for heart failure.
AUTHOR: Doggrell, Sheila A., Dr. (correspondence); Brown, Lindsay
CORPORATE SOURCE: Dept. of Physiology/Pharmacology, School of Biomedical Sciences, The University of Queensland, Brisbane, QLD 4072, Australia. s.doggrell@mailbox.uq.edu.au
SOURCE: Expert Opinion on Pharmacotherapy, (2002) Vol. 3, No. 7, pp. 915-930.
Refs: 129
ISSN: 1465-6566 CODEN: EOPHF7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jul 2002
Last Updated on STN: 25 Jul 2002

AB The pharmacotherapy currently recommended by the American College of Cardiology and the American Heart Association for heart failure (HF) is a diuretic, an angiotensin-converting enzyme inhibitor (ACEI), a β-adrenoceptor antagonist and (usually) digitalis. This current treatment of HF may be improved by optimising the dose of ACEI used, as increasing the dose of lisinopril increases its benefits in HF. Selective angiotensin receptor-1 (AT(1)) antagonists are effective alternatives for those who cannot tolerate ACEIs. AT(1) antagonists may also be used in combination with ACEIs, as some studies have shown cumulative benefits for

the combination. In addition to being used in Stage IV HF patients, in whom it has a marked benefit, spironolactone should be studied in less severe HF and in the presence of β-blockers. The use of carvedilol, extended-release metoprolol and bisoprolol should be extended to severe HF patients as these agents have been shown to decrease mortality in this group. The ancillary properties of carvedilol, particularly antagonism at prejunctional β-adrenoceptors, may give it additional benefits to selective β(1)-adrenoceptor antagonists. Celiprolol and bucindolol are not the β-blockers of choice in HF, as they do not decrease mortality. Although digitalis does not reduce mortality, it remains the only option for a long-term positive inotropic effect, as the long-term use of the phosphodiesterase inhibitors is associated with increased mortality. The calcium sensitising drug levosimendan may be useful in the hospital treatment of decompensated HF to increase cardiac output and improve dyspnoea and fatigue. The antiarrhythmic drug amiodarone should probably be used in patients at high risk of arrhythmic or sudden death, although this treatment may soon be superseded by the more expensive implanted cardioverter defibrillators, which are probably more effective and have fewer side effects. The natriuretic peptide nesiritide has recently been introduced for the hospital treatment of decompensated HF. Novel drugs that may be beneficial in the treatment of HF include the vasopeptidase inhibitors and the selective endothelin-A receptor antagonists but these require much more investigation. However, disappointing results have been obtained in a large clinical trial of the tumour necrosis factor α antagonist etanercept, where no likelihood of a difference between placebo and etanercept was observed. Small clinical trials with recombinant growth hormone to thicken ventricles in dilated cardiomyopathy have given variable results.

L4 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:906809 CAPLUS
DOCUMENT NUMBER: 137:72913
TITLE: Effects of levosimendan, a novel inotropic calcium-sensitizing drug, in experimental septic shock
AUTHOR(S): Oldner, Anders; Konrad, David; Weitzberg, Eddie; Rudehill, Anders; Rossi, Patrik; Wanecek, Michael
CORPORATE SOURCE: Department of Surgical Sciences, Section of Anaesthesiology and Intensive Care Medicine, Karolinska Institute, Stockholm, Swed.
SOURCE: Critical Care Medicine (2001), 29(11), 2185-2193
CODEN: CCMDC7; ISSN: 0090-3493
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Levosimendan is a novel inodilator that improves cardiac contractility by sensitizing troponin C to calcium. This drug has proved to be effective in treating advanced congestive heart failure but has not been evaluated in septic settings. The purpose of the present study was to study the effects of this drug in a porcine model of endotoxemia in a prospective exptl. study. All animals (fourteen land-race pigs) were anesthetized and catheterized for measurement of central and pulmonary hemodynamics. Ultrasonic flow probes were placed around the renal artery and portal vein to measure blood flow. A tonometer was placed in the ileum to measure mucosal pH. Levosimendan was given to six animals as a bolus (200 μg·kg-1) followed by a continuous infusion (200 μg·kg-1-hr-1). Thirty minutes after onset of levosimendan treatment, all animals received endotoxin (20 μg·kg-1-hr-1 for 3 h). At baseline, levosimendan induced a systemic vasodilation with a reduction in blood pressure and an increase in heart rate. A tendency to an increase in cardiac index did

not reach statistical significance (p = .055). Cardiac index and systemic oxygen delivery were markedly improved in the levosimendan group during endotoxemia. Systemic vascular resistance and blood pressure were reduced in the levosimendan group. The latter parameter, however, was only different from the control group during the initial phase of endotoxin shock but not at the late, most pronounced phase of shock. Levosimendan also efficiently attenuated endotoxin-induced pulmonary hypertension. Portal venous blood flow and gut oxygen delivery were improved, but no concomitant reduction in endotoxin-induced intestinal mucosal acidosis was observed Renal blood flow was unaffected, as was the endotoxin-induced increase in plasma endothelin-1-like immunoreactivity. These findings support previous reports of calcium desensitization as a potential component in septic myocardial depression. Furthermore, the vasodilatory properties of this drug were well tolerated in the current model of hypodynamic endotoxin shock, and they may have contributed to improved regional blood flow as seen in the gut as well as improved systemic perfusion by means of reduced biventricular afterload. Pretreatment with levosimendan in pigs subjected to endotoxin shock improved cardiac output and systemic and gut oxygen delivery. In addition, pulmonary hypertension largely was attenuated without any adverse effects on gas exchange. These results are promising in several aspects, but the role of levosimendan in the treating circulatory failure in sepsis remains to be established.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 29 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 1999087642 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9872607
TITLE: Parenteral inotropic support for advanced congestive heart failure.
AUTHOR: Leier C V; Binkley P F
CORPORATE SOURCE: Division of Cardiology, The Ohio State University, College of Medicine and Public Health, Columbus, OH 43210, USA.
SOURCE: Progress in cardiovascular diseases, (1998 Nov-Dec) Vol. 41, No. 3, pp. 207-24. Ref: 111
Journal code: 0376442. ISSN: 0033-0620.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 7 Jan 1999

AB Parenterally administered positive inotropic agents remain an important component of the therapeutics of cardiac dysfunction and failure . Dobutamine, a catechol, remains the prototype of this drug group, but recently has been joined by the phosphodiesterase III inhibitor, milrinone. Compared with dobutamine, milrinone has greater vasodilating-unloading properties. The catecholamine, dopamine, is often used as a parenteral positive inotrope; but at moderate to high dose, it evokes considerable systemic vasoconstriction. At lower doses, dopamine appears to augment renal function. Levosimendan and toborinone, new compounds with several mechanisms of action, are under active clinical investigation and review for approval. Parenteral positive inotropic therapy is indicated for short-term (hours to days) treatment of cardiovascular decompensation secondary to ventricular systolic dysfunction, low-output heart failure. More prolonged or continuous infusion of one of these agents may be necessary as a "pharmacologic bridge" to cardiac transplantation, another definitive

intervention, or more advanced, intense medical therapy. An occasional patient will require a continuous infusion via indwelling venous catheter and portable pump, simply to be able to be discharged from the hospital setting and function in the home environment. Intermittent parenteral inotropic therapy for chronic heart failure has provoked considerable controversy and passion among cardiologists and heart failure specialists; an attempt is made to present this topic in an objective manner.

L4 ANSWER 28 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1996370166 EMBASE
TITLE: Pharmacology of levosimendan: A new myofilament calcium sensitizer.
AUTHOR: Pagel, Paul S.; Warltier, David C., Dr. (correspondence)
CORPORATE SOURCE: Zablocki Vet. Admin. Medical Center, Milwaukee, WI, United States.
AUTHOR: Haikala, Heimo; Toivonen, Marja-Leena; Lehtonen, Lasse
CORPORATE SOURCE: Orion Corporation, Orion Research Center, Espoo, Finland.
AUTHOR: Pentikainen, Pertti J.; Nieminen, Markku S.
CORPORATE SOURCE: First Department of Medicine, Helsinki University Hospital, Helsinki, Finland.
AUTHOR: Papp, Julian Gy
CORPORATE SOURCE: Department of Pharmacology, Albert Szent-Gyorgyi Med. Univ., Szeged, Hungary.
AUTHOR: Warltier, David C., Dr. (correspondence)
CORPORATE SOURCE: Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, United States.
AUTHOR: Warltier, David C., Dr. (correspondence)
CORPORATE SOURCE: Medical College of Wisconsin, MEB, 8701 Watertown Plank Road, Milwaukee, WI 53226, United States.
SOURCE: Cardiovascular Drug Reviews, (1996) Vol. 14, No. 3, pp. 286-316.
Refs: 66
ISSN: 0897-5957 CODEN: CDREEA
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jan 1997
Last Updated on STN: 9 Jan 1997

AB Levosimendan, a new myofilament Ca(2+) sensitizer, enhances myocardial contractility by selectively stabilizing the Ca(2+) bound conformation of cTnC in a Ca(2+)-dependent manner. In contrast to other myofilament Ca(2+) sensitizers, levosimendan does not alter Ca(2+) affinity of cTnC or myosin ATPase activity. Levosimendan -induced inhibition of PDE III may contribute to the positive inotropic actions of this drug at higher concentrations. Myofilament Ca(2+) sensitization and stabilization of the Ca(2+)-bound conformation of cTnC may theoretically delay relaxation. Levosimendan, however, has been demonstrated to enhance relaxation of cardiac muscle. In addition to positive inotropic effects, levosimendan causes venous and arterial vasodilation and improves indices of diastolic performance in the presence of normal left ventricular function. In experimental models of and in patients with left ventricular dysfunction, levosimendan causes beneficial reductions in left ventricular preload and afterload and augments contractility and diastolic function without producing reflex increases in heart rate and myocardial oxygen consumption.

Levosimendan potentiates the positive inotropic effects of dopamine, enhances left ventricular-arterial coupling and mechanical efficiency, and improves the contractile function of stunned myocardium. Levosimendan has a high margin of safety in experimental animals. The toxicity of levosimendan in experimental animals is associated with exacerbation of the pharmacological effects. High doses of levosimendan may adversely affect the establishment and maintenance of pregnancy. Levosimendan does not produce mutagenic effects during organogenesis. Levosimendan is rapidly absorbed from the gastrointestinal tract and has high bioavailability, The elimination half-life of levosimendan is approximately 1 h in patients with heart failure and is not altered in the presence of renal insufficiency. Levosimendan is metabolized by hepatic glutathione conjunction or reduction by intestinal bacteria and is excreted in the urine and feces. High doses of levosimendan may cause headaches and dizziness in healthy volunteers, and to a lesser extent, in patients with congestive heart failure via peripheral vasodilation. The incidence of other adverse drug effects, including hypotension, tachycardia, and palpitations, is low. The clinical utility and safety of levosimendan in patients with congestive heart failure require further investigation.

L4 ANSWER 29 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:47358 BIOSIS
DOCUMENT NUMBER: PREV199698619493
TITLE: The effects of renal failure on the pharmacokinetics of levosimendan.
AUTHOR(S): Sandell, E. P.; Antila, S.; Koisinen, H.; Pentikainen, P. J.
CORPORATE SOURCE: Orion Farmos, Cardiovascular Projects, Orionintie 1, FIN-02700 Espoo, Finland
SOURCE: Therapie (Paris), (1995) Vol. 0, No. SUPPL., pp. 495.
Meeting Info.: 1st Congress of the European Association for Clinical Pharmacology and Therapeutics. Paris, France. September 27-30, 1995.
CODEN: THERAP. ISSN: 0040-5957.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Feb 1996
Last Updated on STN: 2 Feb 1996

=> s (l1 or levosimendan or simdax or simendan) and (renal or kidney) (s) function
L5 50 (L1 OR LEVOSIMENDAN OR SIMDAX OR SIMENDAN) AND (RENAL OR KIDNEY) (S) FUNCTION

=> s l5 and py<=2004
L6 9 L5 AND PY<=2004

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 6 DUP REM L6 (3 DUPLICATES REMOVED)

=> d l7 ibib abs 1-6

L7 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:891335 CAPLUS

DOCUMENT NUMBER: 145:263302
TITLE: Methods of cardioprotection using dichloroacetate in combination with an inotrope
INVENTOR(S): Lopaschuk, Gary D.; Collins-Nakai, Ruth
PATENT ASSIGNEE(S): University of Alberta, Can.
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 13,666.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060194878	A1	20060831	US 2005-229101	20050916
US 6693133	B1	20040217	US 2002-268069	20021007 <--
US 20040162346	A1	20040819	US 2004-778791	20040213 <--
US 7432247	B2	20081007		
US 20050282896	A1	20051222	US 2004-13666	20041215
WO 2006063446	A1	20060622	WO 2005-CA1894	20051215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
WO 2007030944	A2	20070322	WO 2006-CA1523	20060915
WO 2007030944	A3	20070503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				

PRIORITY APPLN. INFO.:		
US 2002-268069	A1	20021007
US 2004-778791	A2	20040213
US 2004-13666	A2	20041215
US 2005-229101	A	20050916

AB The invention provides methods for maintaining or improving cardiac function after a cardiac function disturbing event by the use of cardioprotective dichloroacetate (DCA) and a inotropic drug. The invention also provides pharmaceutical compns. comprising the combination of DCA and inotropic drug, pharmaceutically acceptable carriers and optional other therapeutic agents. Also provided are the dosage protocols for the DCA and inotropic drug combination.

L7 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005065095 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15693696

TITLE: Levosimendan in daily intensive care practice--the experience of 15 centers. Background, methods and organization of the PORTLAND study.

AUTHOR: Cardoso J Silva; Ferreira Jorge; de Sa Edwiges Prazeres; de Campos J Martins; Fonseca Candida; Lousada Nuno; Moreira J Ilidio; Rabacal Carlos; Damasceno Albertino; Seabra-Gomes Ricardo; Ferreira Rafael; Abreu e Lima Cassianosilvacardoso30@hotmail.com

SOURCE: Revista portuguesa de cardiologia : orgao oficial da Sociedade Portuguesa de Cardiologia = Portuguese journal of cardiology : an official journal of the Portuguese Society of Cardiology, (2004 Nov) Vol. 23, No. 11, pp. 1431-43.
Journal code: 8710716. ISSN: 0870-2551.
PUB. COUNTRY: Portugal
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LANGUAGE: English; Portuguese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 8 Feb 2005
Last Updated on STN: 18 Mar 2005
Entered Medline: 17 Mar 2005

AB INTRODUCTION: The LIDO and RUSSLAN trials showed that levosimendan was well tolerated and had a stronger hemodynamic effect than dobutamine and a positive impact on prognosis. There are, however, few data regarding its effectiveness and safety when used in an everyday clinical setting. OBJECTIVE: To test the hypothesis that in day-to-day practice conditions levosimendan is both effective and safe for the treatment of decompensated heart failure (HF). This primary combined endpoint of effectiveness and safety was evaluated at 24 hours and 5 days after the beginning of the treatment. DESIGN: Prospective, multicenter, nonrandomized clinical trial with evaluations at baseline, 24 hours, 5 days, and 3 and 6 months. Follow-up for 6 months. SETTING: The intensive care units of 15 cardiology or internal medicine departments. PATIENTS: 129 consecutive patients requiring inotropes due to decompensated systolic HF despite maximally tolerated oral therapy. Intervention: 24-hour infusion of levosimendan via a central or peripheral vein. MEASUREMENTS AND EVALUATION OF RESULTS: 1. Monitoring: Continuous ECG monitoring, non-invasive blood pressure, urinary output, oximetry. Invasive monitoring was not required. 2. Follow-up. Baseline evaluation: history, physical examination, ECG, 2D echocardiogram, hemogram, ionogram, liver and kidney function. 24-hour and 5-day evaluations: symptoms, physical examination, recording of medical therapy and previous 24-hour urinary output, ECG, hemogram, ionogram, liver and kidney function, and evaluation of arrhythmic episodes and heart rate and blood pressure trends in previous 24 hours. 3- and 6-month evaluations: number of hospital admissions and length of hospital stay due to HF, and mortality. 3. Evaluation of primary endpoint. EFFECTIVENESS: assessed by a clinical score including 2 subjective parameters (1. NYHA functional class, 2. patient self-evaluation symptom class) and 6 objective parameters (3. body weight, 4. pulmonary congestion, 5. previous 24-hour diuresis, 6. serum creatinine, 7. oral HF medication, 8. intravenous HF medication). Definition of clinical effectiveness: improvement in > or = 1 subjective parameters plus improvement in > or = 1 objective parameters, with all other parameters unchanged. Safety: The therapy was judged safe in the absence of any serious adverse event with a probable or undetermined causal relationship with levosimendan. Primary endpoint evaluation: Patients reached the primary endpoint when levosimendan was both effective and safe according to the above definitions.

L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:51937 CAPLUS
DOCUMENT NUMBER: 140:350704
TITLE: Vasoactive drugs and the kidney
AUTHOR(S): Lee, Raymond Wai Chuen; Di Giantomasso, David; May, Clive; Bellomo, Rinaldo
CORPORATE SOURCE: Department of Intensive Care and Department of Medicine, Florey Institute of Physiology, Austin Hospital, Melbourne, Australia
SOURCE: Best Practice & Research, Clinical Anaesthesiology (2004), 18(1), 53-74
CODEN: BPRC08
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Protection of renal function and prevention of acute renal failure (ARF) are important goals of resuscitation in critically ill patients. Beyond fluid resuscitation and avoidance of nephrotoxins, little is known about how such prevention can be achieved. Vasoactive drugs are often administered to improve either cardiac output or mean arterial pressure in the hope that renal blood flow will also be improved and, thereby, renal protection achieved. Some of these drugs (especially low-dose dopamine) have even been proposed to have a specific beneficial effect on renal blood flow. However, when all studies dealing with vasoactive drugs and their effects on the kidney are reviewed, it is clear that none were demonstrated to achieve clin. important benefits in terms of renal protection. It is also clear that, with the exception of low-dose dopamine, there were no randomized controlled trials of sufficient statistical power to detect differences in clin. meaningful outcomes. In the absence of such data, all that is available is based on limited physiol. gains (changes in renal blood flow or urine output) with one or another drug in one or another subpopulation of patients. Furthermore, given the authors' lack of understanding of the pathogenesis of ARF, it is unclear whether hemodynamic manipulation is an appropriate avenue to achieve renal protection. There is a great need for large randomized controlled trials to test the clin., instead of physiol., effects of vasoactive drugs in critical illness.
REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35534 BIOSIS
DOCUMENT NUMBER: PREV200400033328
TITLE: Levosimendan is efficacious in acute heart failure independent of renal function.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author]; Providencia, L. A. [Reprint Author]
CORPORATE SOURCE: Cardiology Dept., Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L7 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35533 BIOSIS
DOCUMENT NUMBER: PREV200400033327
TITLE: Levosimendan is beneficial in diabetics with acute heart failure.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author]; Providencia, L. [Reprint Author]
CORPORATE SOURCE: Cardiology Department, Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 407. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L7 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999087642 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9872607
TITLE: Parenteral inotropic support for advanced congestive heart failure.
AUTHOR: Leier C V; Binkley P F
CORPORATE SOURCE: Division of Cardiology, The Ohio State University, College of Medicine and Public Health, Columbus, OH 43210, USA.
SOURCE: Progress in cardiovascular diseases, (1998 Nov-Dec) Vol. 41, No. 3, pp. 207-24. Ref: 111
Journal code: 0376442. ISSN: 0033-0620.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 7 Jan 1999

AB Parenterally administered positive inotropic agents remain an important component of the therapeutics of cardiac dysfunction and failure. Dobutamine, a catechol, remains the prototype of this drug group, but recently has been joined by the phosphodiesterase III inhibitor, milrinone. Compared with dobutamine, milrinone has greater vasodilating-unloading properties. The catecholamine, dopamine, is often used as a parenteral positive inotrope; but at moderate to high dose, it evokes considerable systemic vasoconstriction. At lower doses, dopamine appears to augment renal function.
Levosimendan and toborinone, new compounds with several mechanisms of action, are under active clinical investigation and review for approval. Parenteral positive inotropic therapy is indicated for short-term (hours to days) treatment of cardiovascular decompensation secondary to ventricular systolic dysfunction, low-output heart failure. More prolonged or continuous infusion of one of these agents may be

necessary as a "pharmacologic bridge" to cardiac transplantation, another definitive intervention, or more advanced, intense medical therapy. An occasional patient will require a continuous infusion via indwelling venous catheter and portable pump, simply to be able to be discharged from the hospital setting and function in the home environment. Intermittent parenteral inotropic therapy for chronic heart failure has provoked considerable controversy and passion among cardiologists and heart failure specialists; an attempt is made to present this topic in an objective manner.

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NEWS 2	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
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NEWS 4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS 5	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents
NEWS 6	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS 7	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus
NEWS 8	OCT 21	Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded
NEWS 9	OCT 21	Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models
NEWS 10	NOV 23	Addition of SCAN format to selected STN databases
NEWS 11	NOV 23	Annual Reload of IFI Databases
NEWS 12	DEC 01	FRFULL Content and Search Enhancements
NEWS 13	DEC 01	DGENE, USGENE, and PCTGEN: new percent identity feature for sorting BLAST answer sets
NEWS 14	DEC 02	Derwent World Patent Index: Japanese FI-TERM thesaurus added
NEWS 15	DEC 02	PCTGEN enhanced with patent family and legal status display data from INPADOCDB
NEWS 16	DEC 02	USGENE: Enhanced coverage of bibliographic and sequence information
NEWS 17	DEC 21	New Indicator Identifies Multiple Basic Patent Records Containing Equivalent Chemical Indexing in CA/CAplus
NEWS 18	JAN 12	Match STN Content and Features to Your Information Needs, Quickly and Conveniently
NEWS 19	JAN 25	Annual Reload of MEDLINE database

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=> e levosimendaon
E1            1     LEVOSEMOTIADIL/BI
E2            1     LEVOSIMENDAN/BI
E3            0 --> LEVOSIMENDAON/BI
E4            1     LEVOSIN/BI
E5            1     LEVOSINUM/BI
E6            1     LEVOSPASME/BI
E7            1     LEVOSTARCH/BI
E8            1     LEVOSULFIN/BI
E9            1     LEVOSULP/BI
E10           1     LEVOSULPIRID/BI
E11           1     LEVOSULPIRIDE/BI
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E12          4     LEVOTAN/BI

=> s e2
L1           1 LEVOSIMENDAN/BI

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2010 ACS on STN
RN   141505-33-1  REGISTRY
ED   Entered STN:  22 May 1992
CN   Propanedinitrile, 2-[2-[4-[(4R)-1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl]phenyl]hydrazinylidene]-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Propanedinitrile, [[4-(1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl)phenyl]hydrazono]-, (R)-
CN   Propanedinitrile, [[4-[(4R)-1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl]phenyl]hydrazono]- (9CI)
OTHER NAMES:
CN   (-)-OR 1259
CN   (R)-Simendan
CN   Levosimendan
CN   OR 1259
CN   Simdax
FS   STEREOSEARCH
MF   C14 H12 N6 O
CI   COM
SR   World Health Organization (WHO)
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
       CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE,
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       USPATFULL
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Absolute stereochemistry.
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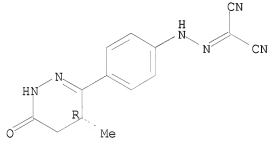


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               6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             408 REFERENCES IN FILE CAPLUS (1907 TO DATE)


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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
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=> s (l1 or levosimendan) and (renal or kidney)
L2          216 (L1 OR LEVOSIMENDAN) AND (RENAL OR KIDNEY)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3          172 DUP REM L2 (44 DUPLICATES REMOVED)

=> s l3 not py>2003
L4           18 L3 NOT PY>2003

=> d l4 ibib abs 1-18

L4   ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:         2001:906809  CAPLUS
DOCUMENT NUMBER:          137:72913
TITLE:                    Effects of levosimendan, a novel inotropic
                          calcium-sensitizing drug, in experimental septic shock
AUTHOR(S):                Oldner, Anders; Konrad, David; Weitzberg, Eddie;
                          Rudehill, Anders; Rossi, Patrik; Wanecek, Michael
CORPORATE SOURCE:         Department of Surgical Sciences, Section of
                          Anaesthesiology and Intensive Care Medicine,
                          Karolinska Institute, Stockholm, Swed.
SOURCE:                   Critical Care Medicine (2001), 29(11), 2185-2193
                          CODEN: CCMDC7; ISSN: 0090-3493
PUBLISHER:                Lippincott Williams & Wilkins
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Levosimendan is a novel inodilator that improves cardiac
     contractility by sensitizing troponin C to calcium.  This drug has proved
     to be effective in treating advanced congestive heart failure but has not
     been evaluated in septic settings.  The purpose of the present study was
     to study the effects of this drug in a porcine model of endotoxemia in a
     prospective exptl. study.  All animals (fourteen land-race pigs) were
     anesthetized and catheterized for measurement of central and pulmonary
     hemodynamics.  Ultrasonic flow probes were placed around the renal
     artery and portal vein to measure blood flow.  A tonometer was placed in
     the ileum to measure mucosal pH.  Levosimendan was given to six
     animals as a bolus (200 μg·kg-1) followed by a continuous
     infusion (200 μg·kg-1-hr-1).  Thirty minutes after onset of
     levosimendan treatment, all animals received endotoxin (20
     μg·kg-1-hr-1 for 3 h).  At baseline,  levosimendan
     induced a systemic vasodilation with a reduction in blood pressure and an
     increase in heart rate.  A tendency to an increase in cardiac index did
     not reach statistical significance (p = .055).  Cardiac index and systemic
     oxygen delivery were markedly improved in the levosimendan group
     during endotoxemia.  Systemic vascular resistance and blood pressure were
     reduced in the levosimendan group.  The latter parameter,
     however, was only different from the control group during the initial
```

phase of endotoxin shock but not at the late, most pronounced phase of shock. Levosimendan also efficiently attenuated endotoxin-induced pulmonary hypertension. Portal venous blood flow and gut oxygen delivery were improved, but no concomitant reduction in endotoxin-induced intestinal mucosal acidosis was observed Renal blood flow was unaffected, as was the endotoxin-induced increase in plasma endothelin-1-like immunoreactivity. These findings support previous reports of calcium desensitization as a potential component in septic myocardial depression. Furthermore, the vasodilatory properties of this drug were well tolerated in the current model of hypodynamic endotoxin shock, and they may have contributed to improved regional blood flow as seen in the gut as well as improved systemic perfusion by means of reduced biventricular afterload. Pretreatment with levosimendan in pigs subjected to endotoxin shock improved cardiac output and systemic and gut oxygen delivery. In addition, pulmonary hypertension largely was attenuated without any adverse effects on gas exchange. These results are promising in several aspects, but the role of levosimendan in the treating circulatory failure in sepsis remains to be established.

OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1996:619297 CAPLUS

DOCUMENT NUMBER: 125:265511

ORIGINAL REFERENCE NO.: 125:49277a,49280a

TITLE: Influence of levosimendan, pimobendan, and milrinone on the regional distribution of cardiac output in anesthetized dogs

AUTHOR(S): Pagel, Paul S.; Hettrick, Douglas A.; Warltier, David C.

CORPORATE SOURCE: Dep. Anesthesiol., Med. Coll. Wisconsin, Milwaukee, WI, 53226, USA

SOURCE: British Journal of Pharmacology (1996), 119(3), 609-615
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The distribution of cardiac output during administration of levosimendan, a new myofilament calcium sensitizer, is unknown. The authors examined and compared the effects of levosimendan, pimobendan, and milrinone on regional tissue perfusion by use of the radioactive microsphere technique in barbiturate-anesthetized dogs. Hemodynamics and regional blood flow were determined before and during infusions of levosimendan (0.75, 1.5, and 3.0 μg kg-1 min-1), pimobendan (10, 20, and 40 μg kg-1 min-1), or milrinone (1.0, 2.0, and 4.0 μg kg-1 min-1). All three drugs caused similar increases in heart rate, cardiac output, and left ventricular + dP/dt and decreases in end-diastolic pressure and systemic vascular resistance. No changes in subendocardial, midmyocardial, and subepicardial blood flow occurred during administration of levosimendan. However, a redistribution of blood flow from subendocardium to subepicardium was observed Pimobendan increased midmyocardial. and subepicardial blood flow and reduced the endo/epi ratio to a greater degree than levosimendan. Milrinone did not affect myocardial perfusion. Levosimendan increased blood flow to the renal medulla and decreased renal medullary and cortical vascular resistance. Levosimendan increased blood flow to the small intestine and liver and reduced vascular resistance in these organs. Pimobendan increased hepatic blood flow to a greater degree than levosimendan but did

not alter small intestinal perfusion. All three drugs decreased splenic blood flow to similar degrees. Levosimendan and pimobendan reduced cerebral vascular resistance. Levosimendan and milrinone reduced skeletal muscle vascular resistance. The results indicate that levosimendan, pimobendan, and milrinone cause subtlety different alterations in regional tissue perfusion while producing similar hemodynamics effects.

OS.CITING REF COUNT: 34 THERE ARE 34 CAPLUS RECORDS THAT CITE THIS RECORD (34 CITINGS)

L4 ANSWER 3 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1999087642 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9872607
TITLE: Parenteral inotropic support for advanced congestive heart failure.
AUTHOR: Leier C V; Binkley P F
CORPORATE SOURCE: Division of Cardiology, The Ohio State University, College of Medicine and Public Health, Columbus, OH 43210, USA.
SOURCE: Progress in cardiovascular diseases, (1998 Nov-Dec) Vol. 41, No. 3, pp. 207-24. Ref: 111
Journal code: 0376442. ISSN: 0033-0620. L-ISSN: 0033-0620.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 7 Jan 1999

AB Parenterally administered positive inotropic agents remain an important component of the therapeutics of cardiac dysfunction and failure. Dobutamine, a catechol, remains the prototype of this drug group, but recently has been joined by the phosphodiesterase III inhibitor, milrinone. Compared with dobutamine, milrinone has greater vasodilating-unloading properties. The catecholamine, dopamine, is often used as a parenteral positive inotrope; but at moderate to high dose, it evokes considerable systemic vasoconstriction. At lower doses, dopamine appears to augment renal function. Levosimendan and toborinone, new compounds with several mechanisms of action, are under active clinical investigation and review for approval. Parenteral positive inotropic therapy is indicated for short-term (hours to days) treatment of cardiovascular decompensation secondary to ventricular systolic dysfunction, low-output heart failure. More prolonged or continuous infusion of one of these agents may be necessary as a "pharmacologic bridge" to cardiac transplantation, another definitive intervention, or more advanced, intense medical therapy. An occasional patient will require a continuous infusion via indwelling venous catheter and portable pump, simply to be able to be discharged from the hospital setting and function in the home environment. Intermittent parenteral inotropic therapy for chronic heart failure has provoked considerable controversy and passion among cardiologists and heart failure specialists; an attempt is made to present this topic in an objective manner.

L4 ANSWER 4 OF 18 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35535 BIOSIS
DOCUMENT NUMBER: PREV200400033329
TITLE: Prognostic markers of levosimendan treatment efficacy in severe congestive heart failure: A prospective multicentre Study.
AUTHOR(S): Bocchi, E. [Reprint Author]; Guimaraes, G. [Reprint Author]; Vilas-Boas, F.

CORPORATE SOURCE: Medical School, Heart Institute (InCor), University of Sao Paulo, Sao Paulo, Brazil
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L4 ANSWER 5 OF 18 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35534 BIOSIS
DOCUMENT NUMBER: PREV200400033328
TITLE: Levosimendan is efficacious in acute heart failure independent of renal function.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author]; Providencia, L. A. [Reprint Author]
CORPORATE SOURCE: Cardiology Dept., Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L4 ANSWER 6 OF 18 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35533 BIOSIS
DOCUMENT NUMBER: PREV200400033327
TITLE: Levosimendan is beneficial in diabetics with acute heart failure.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author]; Providencia, L. [Reprint Author]
CORPORATE SOURCE: Cardiology Department, Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 407. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L4 ANSWER 7 OF 18 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:15784 BIOSIS
DOCUMENT NUMBER: PREV200400013587
TITLE: Development of a comprehensive new endpoint for the evaluation of new treatments for acute decompensated heart failure: Results with levosimendan in the REVIVE-1 Study.
AUTHOR(S): Packer, M. [Reprint Author]; Colucci, W. S.; Fisher, L.; Massie, B. M.; Teerlink, J. R.; Young, J. B.; Garratt, C.
CORPORATE SOURCE: Medicine, Columbia University, New York, NY, USA
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 24. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

L4 ANSWER 8 OF 18 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:47358 BIOSIS
DOCUMENT NUMBER: PREV199698619493
TITLE: The effects of renal failure on the pharmacokinetics of levosimendan.
AUTHOR(S): Sandell, E. P.; Antila, S.; Koisinen, H.; Pentikainen, P. J.
CORPORATE SOURCE: Orion Farmos, Cardiovascular Projects, Orionintie 1, FIN-02700 Espoo, Finland
SOURCE: Therapie (Paris), (1995) Vol. 0, No. SUPPL., pp. 495.
Meeting Info.: 1st Congress of the European Association for Clinical Pharmacology and Therapeutics. Paris, France. September 27-30, 1995.
CODEN: THERAP. ISSN: 0040-5957.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Feb 1996
Last Updated on STN: 2 Feb 1996

L4 ANSWER 9 OF 18 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003494488 EMBASE
TITLE: Clinical decision making in managing the 'difficult' patient with chronic heart failure: Who, when, how, where?.
AUTHOR: Krum, Henry, Prof. (correspondence)
CORPORATE SOURCE: Dept. of Epidemiol. and Prev. Med., Monash Univ. Ctrl. and E. Clin. Sch., Alfred Hospital, Melbourne, Vic. 3004, Australia.
SOURCE: European Heart Journal, Supplement, (Dec 2003) Vol. 5, No. I, pp. I88-I96.
Refs: 58
ISSN: 1520-765X CODEN: EHJSFT
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Dec 2003
Last Updated on STN: 30 Dec 2003

AB Chronic heart failure (CHF) is a complex disorder, and all patients with this condition could therefore be considered 'difficult'. Nevertheless, there are certain subgroups in whom management poses greater challenges. These include patients with advanced disease severity, complications arising from CHF, comorbidities, and patients in whom it is difficult to optimize standard therapies. Advanced disease is associated with reduced quality of life, frequent hospitalization and poor survival. Major challenges in advanced CHF include ensuring adequate tolerability of therapy, keeping patients out of hospital and decision making regarding palliation. Complications such as tachyarrhythmias and bradyarrhythmias may also alter management. CHF is a pro-thromboembolic state, but the role of anticoagulation and antiplatelet therapy is unclear. Weight loss is an independent prognostic marker for poor survival in complicated CHF, and therapies directed at reducing weight loss may improve outcome. Comorbid conditions that may affect decision making in the patient with CHF include aetiological contributors (e.g. ischaemic heart disease, hypertension, diabetes mellitus and anaemia) and other comorbid disorders such as respiratory disease, cognitive dysfunction, depression, renal failure and arthritis. In some clinical scenarios, optimal therapy may not easily be achieved. In patients with low systemic blood pressure, vasodilating drugs may be difficult to use. Bradyarrhythmias or bronchial hyperreactivity may limit the use of beta-blockers. Drug therapy may also be difficult to optimize in patients with advanced renal dysfunction. .COPYRGT. 2003 The European Society of Cardiology. Published by Elsevier Science Ltd.

L4 ANSWER 10 OF 18 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003301348 EMBASE
TITLE: Clinical use of inotropic therapy for heart failure: Looking backward or forward? Part I: Inotropic infusions during hospitalization.
AUTHOR: Stevenson, Lynne Warner, Dr. (correspondence)
CORPORATE SOURCE: Division of Cardiology, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115, United States.
SOURCE: Circulation, (22 Jul 2003) Vol. 108, No. 3, pp. 367-372. Refs: 50
ISSN: 0009-7322 CODEN: CIRCAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Aug 2003
Last Updated on STN: 14 Aug 2003

L4 ANSWER 11 OF 18 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003256920 EMBASE
TITLE: Gateways to clinical trials: May 2003.
AUTHOR: Bayes, M. (correspondence)
CORPORATE SOURCE: Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
AUTHOR: Rabasseda, X.; Prous, J.R.

SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (May 2003) Vol. 25, No. 4, pp. 317-340.
Refs: 143
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2003
Last Updated on STN: 17 Jul 2003

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity®, the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: 2F5, 2G12, Abetimus sodium, ABI-007, adalimumab, adefovir dipivoxil, AE-941, alefacept, altropane, aminolevulinic acid hydrochloride, aminolevulinic acid methyl ester, aminopterin, anakinra, aprinocarsen sodium, atazanavir, atlizumab, atomoxetine hydrochloride; B7-1 vaccine, bevacizumab, biricodar dicitrate, BMS-188667, brasofensine sulfate, bryostatin 1; Cantuzumab mertansine, CHS-828, cinacalcet hydrochloride, cipamfylline, creatine, CVT-3146; Darbepoetin alfa, DITPA, drotrecogin alfa (activated), duloxetine hydrochloride; Edatrexate, efalizumab, ENMD-0997, epoetin, erlosamide, esomeprazole magnesium, etiprednol dicloacetate, etoricoxib, everolimus, ezetimibe; Fampridine, fenretinide, FTY-720; IGF-I/IGFBP-3 IL-1 cytokine trap, ilodecakin, interferon beta, ISIS-104838, ISIS-2503, ISIS-5132, ivabradine hydrochloride; Lafutidine, lanthanum carbonate, L-Arginine hydrochloride, LEA29Y, lerdelimumab, levetiracetam, levobupivacaine hydrochloride, levosimendan, lopinavir; Melagatran, mibefradil hydrochloride, miglustat, morphine-6-glucuronide; Nesiritide; Omalizumab, omapatrilat; p24-VLP, parecoxib sodium, peginterferon alfa-2a, peginterferon alfa-2b, pegsunercept, pitavastatin calcium, plevitrexed, prasterone, pregabalin, PRO-2000, prucalopride; Rapacuronium bromide, rebimastat, RGA-0853, rubitecan, ruboxistaurin mesilate hydrate, RWJ-67657; S-16020-2, sarizotan, SLV-306, stiripentol; TA-CIN, tenecteplase, teriparatide, tezacitabine, tipifarnib, trabectedin, troglitazone; Valdecoxib, vardenafil; Z-338, ziconotide. .COPYRGT. 2003 Prous Science. All rights reserved.

L4 ANSWER 12 OF 18 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003158036 EMBASE
TITLE: [Cardiac failure in intensive care].
Srdecni selhani v intenzivni peci.
AUTHOR: Parizkova, R., Dr. (correspondence)
CORPORATE SOURCE: Univerzita Karlova v Praze, Lekarska Fakulta v Hradci Kralove, Fakultni Nemocnice Hradec Kralove, 500 05 Hradec Kralove, Czech Republic.
AUTHOR: Parizkova, R., Dr. (correspondence)
CORPORATE SOURCE: Klin. Anesteziol. Resuscitace/I. M., Fakultni Nemocnice, 500 05 Hradec Kralove, Czech Republic.
SOURCE: Anesteziologie a Neodkladna Pece, (2003) Vol. 14, No. 2, pp. 103-110.
Refs: 27
ISSN: 0862-4968 CODEN: ANPEFF
COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
024 Anesthesiology

036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: Czech
SUMMARY LANGUAGE: English; Czech
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 1 May 2003

AB Heart failure represents almost 5 % of all hospital admissions and both mortality and health care cost on account of those patients are high. The proportion of patients on ICU with heart failure of various origin (mostly as a results either of primary heart damage or as a result of secondary heart damage due to multiple organ failure) has increased rapidly during the last two decades. Heart failure occurs mostly as a result of ischaemic heart disease and the prevalence of heart failure increases in those with both ischaemic heart disease and hypertension. Increased sympathetic activity, renin-angiotensin-aldosterone axis, vasopressin, endothelin and atrial natriuretic peptides play the most important role in developing heart failure. Current definitions, diagnosis and recommended treatment of heart failure are based on recommendation issued by European Society of Cardiology. Echocardiography together with assessment of atrial natriuretic peptide plasma levels are preferred methods for diagnosis. The current therapeutic approach to heart failure is stratified according to levels of evidence based medicine methodology. The control of underlying cause and optimizing of myocardial oxygen delivery to failing heart without increasing oxygen consumption at the same time represent the cornerstone of therapy in heart failure patients. Diuretics, vasodilators together with inotropic agents (dobutamine, phosphodiesterase inhibitors and recently calcium sensitizers, if necessary), are the most recommended drugs in this setting. ACE inhibitors and beta-blockers are the key agents for long-term pharmacological therapy in chronic heart failure patients. Non-pharmacological modalities are also mentioned.

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ACCESSION NUMBER: 2003156768 EMBASE
TITLE: Projecting future drug expenditures - 2003.
AUTHOR: Shah, Nilay D.; Vermeulen, Lee C. (correspondence)
CORPORATE SOURCE: Center for Drug Policy, Univ. of Wisconsin Hosp. and Clinics, 600 Highland Avenue, Madison, WI 53792, United States.
AUTHOR: Shah, Nilay D.
CORPORATE SOURCE: Dept. of Population Health Sciences, School of Medicine, Univ. Wisconsin-Madison (UW-Madison), Madison, WI, United States.
AUTHOR: Hoffman, James M.
CORPORATE SOURCE: Outcomes Res./Medication Use Policy, UWHC, Madison, WI, United States.
AUTHOR: Vermeulen, Lee C. (correspondence)
CORPORATE SOURCE: School of Pharmacy, UW-Madison, Madison, WI, United States.
AUTHOR: Hunkler, Robert J.; Hontz, Karrie M.
CORPORATE SOURCE: Business Development, IMS HEALTH, Plymouth Meeting, PA, United States.
SOURCE: American Journal of Health-System Pharmacy, (15 Jan 2003) Vol. 60, No. 2, pp. 137-149.
Refs: 46
ISSN: 1079-2082 CODEN: AHSPEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 1 May 2003

AB Drug expenditure projections for 2003 and factors likely to influence drug costs are discussed. The United States continues to face the challenge of increased growth in health expenditures, and drug expenditures are continuing to increase faster than the growth in total health care expenditures. These increases can be largely attributed to an increase in the average age of the U.S. population and technological advancement. On the basis of price inflation and non-price inflationary factors, including increases in volume, shifts in patient and therapeutic intensity, and expected approval of new drugs, a 10-12% increase in drug expenditures in 2003 for the inpatient setting and a 13.5-15.5% increase for ambulatory care settings are forecasted. While few new drugs are expected to greatly influence expenditures in 2003, the continued diffusion of recently approved drugs such as drotrecogin alfa and nesiritide will have a dramatic impact on total drug expenditures and must be carefully considered in the budgeting process. An agent likely to have a significant impact on HIV treatment is enfuvirtide, the first in a new class of antiretrovirals (fusion inhibitors), but its high cost ($10,000-$15,000 per year) may limit patients' access to this medication. An expanded user's guide is provided to assist the reader in appropriate application of this information in the drug budgeting process. Technological, demographic, and market-based changes and changes in public policy will continue to influence pharmaceutical expenditures in the coming year. An understanding of the overall drivers of medication expenditures and vigilance in monitoring pharmaceutical innovation are critical in the effective management of these resources.

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ACCESSION NUMBER: 2003148612 EMBASE
TITLE: Gateways to clinical trials.
AUTHOR: Bayes, M. (correspondence)
CORPORATE SOURCE: P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
AUTHOR: Rabasseda, X.; Prous, J.R.
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (Mar 2003) Vol. 25, No. 2, pp. 145-168. Refs: 149
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 028 Urology and Nephrology
030 Clinical and Experimental Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2003
Last Updated on STN: 24 Apr 2003

AB Gateways to clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity®, the drug discovery and devlopment protal, http://integrity.prous.com. This issue focuses on the following selection of drugs: AAV-CF, adalimumab, ademetionine, afeletecan hydrochloride, agomelatine, alemtuzumab, almotriptan, amdoxovir, aplidine, aranose, arsenic sulfide, atazanavir, atlizumab; Bimatoprost, BMS-181176, BMS-188667, bortezomib, bryostatin 1; Combretastatin A-4 phosphate; Darbepoetin alfa, darusentan, deferasirox, desloratadine,

DTaP-HBV-IPV/Hib-vaccine, DTI-0009; Eculizumab, edodekin alfa, emtricitabine, enfuvirtide, epoetin, esomeprazole magnesium etoricoxib; Fampridine, fenretinide, FR-146687; Galiximab, gamma-Hydroxybutyrate sodium, ganirelix acetate, gefitinib, Gemtuzumab ozogamicin, gimatecan; HEA125xOKT3, hIL-13-PE38QQR, HSV-2 theracine, Hu14.18-IL-2, human gammaglobulin; Idraparinux sodium, imatinib mesylate; IMiD3, insulin detemir, interleukin-4, irofulven, ISAtx-247; JT-1001; Levetiracetam, levosimendan, liposomal doxorubicin, liposomal vincristine sulfate, lixivaptan, lopinavir, lumiracoxib; Maxacalcitol, melatonin, midostaurin, MLN-518; Neridronic acid, nesiritide, nitronaproxen; Oblimersen sodium, oregovomab; PEG-filgrastim, polyglutamate paclitaxel, prasterone, pregabalin; Rosuvastatin calcium, rotigotine hydrochloride; SGN-30; T-1249, tenofovir disoproxil fumarate, teriparatide, tiotropium bromide, tipranavir, TMC-114, trabectedin, transdermal selegiline; UK-427857; Valdecoxib, valganciclovir hydrochloride, vardenafil, vatalanib succinate, vincristine sulfate TCS; Zofenopril calcium. .COPYRGT. 2003 Prous Science. All rights reserved.

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ACCESSION NUMBER:	2003075961 EMBASE
TITLE:	15th Annual Congress of the European Society of Intensive Care Medicine, 29 September-2 October 2002, Barcelona, Spain: Clinical research to improve outcome.
AUTHOR:	Dubois, Marc-Jacques (correspondence); Bouali, Redouane
CORPORATE SOURCE:	Critical Care Medicine Division, University of Montreal Hospital, Montreal, Que., Canada. marc-jacques.dubois@umontreal.ca
AUTHOR:	Verdant, Colin L.
CORPORATE SOURCE:	Faculty of Medicine, University of Montreal, Montreal, Que., Canada.
SOURCE:	Critical Care, (Feb 2003) Vol. 7, No. 1, pp. 91-94. Refs: 12 ISSN: 1364-8535 CODEN: CRCAFM
COUNTRY:	United Kingdom
DOCUMENT TYPE:	Journal; Conference Article; (Conference paper)
FILE SEGMENT:	015 Chest Diseases, Thoracic Surgery and Tuberculosis 018 Cardiovascular Diseases and Cardiovascular Surgery 024 Anesthesiology 028 Urology and Nephrology 037 Drug Literature Index 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE:	English
ENTRY DATE:	Entered STN: 27 Feb 2003 Last Updated on STN: 27 Feb 2003

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ACCESSION NUMBER:	2002247703 EMBASE
TITLE:	Present and future pharmacotherapy for heart failure.
AUTHOR:	Doggrell, Sheila A., Dr. (correspondence); Brown, Lindsay
CORPORATE SOURCE:	Dept. of Physiology/Pharmacology, School of Biomedical Sciences, The University of Queensland, Brisbane, QLD 4072, Australia. s.doggrell@mailbox.uq.edu.au
SOURCE:	Expert Opinion on Pharmacotherapy, (2002) Vol. 3, No. 7, pp. 915-930. Refs: 129 ISSN: 1465-6566 CODEN: EOPHF7
COUNTRY:	United Kingdom
DOCUMENT TYPE:	Journal; General Review; (Review)
FILE SEGMENT:	018 Cardiovascular Diseases and Cardiovascular Surgery

030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jul 2002
Last Updated on STN: 25 Jul 2002

AB The pharmacotherapy currently recommended by the American College of Cardiology and the American Heart Association for heart failure (HF) is a diuretic, an angiotensin-converting enzyme inhibitor (ACEI), a β-adrenoceptor antagonist and (usually) digitalis. This current treatment of HF may be improved by optimising the dose of ACEI used, as increasing the dose of lisinopril increases its benefits in HF. Selective angiotensin receptor-1 (AT1) antagonists are effective alternatives for those who cannot tolerate ACEIs. AT1 antagonists may also be used in combination with ACEIs, as some studies have shown cumulative benefits for the combination. In addition to being used in Stage IV HF patients, in whom it has a marked benefit, spironolactone should be studied in less severe HF and in the presence of β-blockers. The use of carvedilol, extended-release metoprolol and bisoprolol should be extended to severe HF patients as these agents have been shown to decrease mortality in this group. The ancillary properties of carvedilol, particularly antagonism at prejunctional β-adrenoceptors, may give it additional benefits to selective β1-adrenoceptor antagonists. Celiprolol and bucindolol are not the β-blockers of choice in HF, as they do not decrease mortality. Although digitalis does not reduce mortality, it remains the only option for a long-term positive inotropic effect, as the long-term use of the phosphodiesterase inhibitors is associated with increased mortality. The calcium sensitising drug levosimendan may be useful in the hospital treatment of decompensated HF to increase cardiac output and improve dyspnoea and fatigue. The antiarrhythmic drug amiodarone should probably be used in patients at high risk of arrhythmic or sudden death, although this treatment may soon be superseded by the more expensive implanted cardioverter defibrillators, which are probably more effective and have fewer side effects. The natriuretic peptide nesiritide has recently been introduced for the hospital treatment of decompensated HF. Novel drugs that may be beneficial in the treatment of HF include the vasopeptidase inhibitors and the selective endothelin-A receptor antagonists but these require much more investigation. However, disappointing results have been obtained in a large clinical trial of the tumour necrosis factor α antagonist etanercept, where no likelihood of a difference between placebo and etanercept was observed. Small clinical trials with recombinant growth hormone to thicken ventricles in dilated cardiomyopathy have given variable results.

L4 ANSWER 17 OF 18 EMBASE

ACCESSION NUMBER: 2002164027 EMBASE
TITLE: New therapeutic options in congestive heart failure: Part I.
AUTHOR: McMurray, John, Dr. (correspondence); Pfeffer, Marc A.
CORPORATE SOURCE: Clin. Res. Initiative Heart Failure, University of Glasgow, Wolfson Building, Glasgow G12 8QQ, United Kingdom.
SOURCE: Circulation, (30 Apr 2002) Vol. 105, No. 17, pp. 2099-2106. Refs: 72
ISSN: 0009-7322 CODEN: CIRCAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English

ENTRY DATE: Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002

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ACCESSION NUMBER: 1996370166 EMBASE
TITLE: Pharmacology of levosimendan: A new myofilament calcium sensitizer.
AUTHOR: Pagel, Paul S.; Warltier, David C., Dr. (correspondence)
CORPORATE SOURCE: Zablocki Vet. Admin. Medical Center, Milwaukee, WI, United States.
AUTHOR: Haikala, Heimo; Toivonen, Marja-Leena; Lehtonen, Lasse
CORPORATE SOURCE: Orion Corporation, Orion Research Center, Espoo, Finland.
AUTHOR: Pentikainen, Pertti J.; Nieminen, Markku S.
CORPORATE SOURCE: First Department of Medicine, Helsinki University Hospital, Helsinki, Finland.
AUTHOR: Papp, Julian Gy
CORPORATE SOURCE: Department of Pharmacology, Albert Szent-Gyorgyi Med. Univ., Szeged, Hungary.
AUTHOR: Warltier, David C., Dr. (correspondence)
CORPORATE SOURCE: Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, United States.
AUTHOR: Warltier, David C., Dr. (correspondence)
CORPORATE SOURCE: Medical College of Wisconsin, MEB, 8701 Watertown Plank Road, Milwaukee, WI 53226, United States.
SOURCE: Cardiovascular Drug Reviews, (1996) Vol. 14, No. 3, pp. 286-316.
Refs: 66
ISSN: 0897-5957 CODEN: CDREEA
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jan 1997
Last Updated on STN: 9 Jan 1997

AB Levosimendan, a new myofilament Ca2+ sensitizer, enhances myocardial contractility by selectively stabilizing the Ca2+ bound conformation of cTnC in a Ca2+-dependent manner. In contrast to other myofilament Ca2+ sensitizers, levosimendan does not alter Ca2+ affinity of cTnC or myosin ATPase activity. Levosimendan -induced inhibition of PDE III may contribute to the positive inotropic actions of this drug at higher concentrations. Myofilament Ca2+ sensitization and stabilization of the Ca2+-bound conformation of cTnC may theoretically delay relaxation. Levosimendan, however, has been demonstrated to enhance relaxation of cardiac muscle. In addition to positive inotropic effects, levosimendan causes venous and arterial vasodilation and improves indices of diastolic performance in the presence of normal left ventricular function. In experimental models of and in patients with left ventricular dysfunction, levosimendan causes beneficial reductions in left ventricular preload and afterload and augments contractility and diastolic function without producing reflex increases in heart rate and myocardial oxygen consumption. Levosimendan potentiates the positive inotropic effects of dopamine, enhances left ventricular-arterial coupling and mechanical efficiency, and improves the contractile function of stunned myocardium. Levosimendan has a high margin of safety in experimental animals. The toxicity of levosimendan in experimental animals is associated with exacerbation of the pharmacological effects. High doses

of levosimendan may adversely affect the establishment and maintenance of pregnancy. Levosimendan does not produce mutagenic effects during organogenesis. Levosimendan is rapidly absorbed from the gastrointestinal tract and has high bioavailability, The elimination half-life of levosimendan is approximately 1 h in patients with heart failure and is not altered in the presence of renal insufficiency. Levosimendan is metabolized by hepatic glutathione conjunction or reduction by intestinal bacteria and is excreted in the urine and feces. High doses of levosimendan may cause headaches and dizziness in healthy volunteers, and to a lesser extent, in patients with congestive heart failure via peripheral vasodilation. The incidence of other adverse drug effects, including hypotension, tachycardia, and palpitations, is low. The clinical utility and safety of levosimendan in patients with congestive heart failure require further investigation.

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NEWS 4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS 5	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents
NEWS 6	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS 7	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus
NEWS 8	OCT 21	Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded
NEWS 9	OCT 21	Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models
NEWS 10	NOV 23	Addition of SCAN format to selected STN databases
NEWS 11	NOV 23	Annual Reload of IFI Databases
NEWS 12	DEC 01	FRFULL Content and Search Enhancements
NEWS 13	DEC 01	DGENE, USGENE, and PCTGEN: new percent identity feature for sorting BLAST answer sets
NEWS 14	DEC 02	Derwent World Patent Index: Japanese FI-TERM thesaurus added
NEWS 15	DEC 02	PCTGEN enhanced with patent family and legal status display data from INPADOCDB
NEWS 16	DEC 02	USGENE: Enhanced coverage of bibliographic and sequence information
NEWS 17	DEC 21	New Indicator Identifies Multiple Basic Patent

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                    in CA/CAplus
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                    Needs, Quickly and Conveniently
NEWS 19   JAN 25    Annual Reload of MEDLINE database
NEWS 20   FEB 16    STN Express Maintenance Release, Version 8.4.2, Is
                    Now Available for Download
NEWS 21   FEB 16    Derwent World Patents Index (DWPI) Revises Indexing
                    of Author Abstracts
NEWS 22   FEB 16    New FASTA Display Formats Added to USGENE and PCTGEN
NEWS 23   FEB 16    INPADOCDB and INPAFAMDB Enriched with New Content
                    and Features
NEWS 24   FEB 16    INSPEC Adding Its Own IPC codes and Author's E-mail
                    Addresses

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             AND CURRENT DISCOVER FILE IS DATED 15 JANUARY 2010.

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specific topic.

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                                                           ENTRY    SESSION
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DICTIONARY FILE UPDATES:  18 FEB 2010  HIGHEST RN 1206874-44-3

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=> e levosimendan
E1            1     LEVOSEMOTIADI/BI
E2            1     LEVOSEMOTIADIL/BI
E3            1 --> LEVOSIMENDAN/BI
E4            1     LEVOSIN/BI
E5            1     LEVOSINUM/BI
E6            1     LEVOSPASME/BI
E7            1     LEVOSTARCH/BI
E8            1     LEVOSULFIN/BI
E9            1     LEVOSULP/BI
E10           1     LEVOSULPIRID/BI
E11           1     LEVOSULPIRIDE/BI
E12           4     LEVOTAN/BI

=> s e3
L1            1 LEVOSIMENDAN/BI

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2010 ACS on STN
RN   141505-33-1  REGISTRY
ED   Entered STN:  22 May 1992
CN   Propanedinitrile, 2-[2-[4-[(4R)-1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl]phenyl]hydrazinylidene]-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Propanedinitrile, [[4-(1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl)phenyl]hydrazono]-, (R)-
CN   Propanedinitrile, [[4-[(4R)-1,4,5,6-tetrahydro-4-methyl-6-oxo-3-
     pyridazinyl]phenyl]hydrazono]- (9CI)
OTHER NAMES:
CN   (-)-OR 1259
CN   (R)-Simendan
CN   Levosimendan
CN   OR 1259
CN   Simdax
FS   STEREOSEARCH
MF   C14 H12 N6 O
CI   COM
SR   World Health Organization (WHO)
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
       CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE,
       IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*,
       PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)

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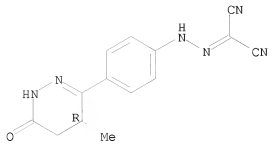

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6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
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FULL ESTIMATED COST                                       8.09       8.31

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=> s (l1 or levosimendan or simdax)
L2        2673 (L1 OR LEVOSIMENDAN OR SIMDAX)

=> s l2 not py>2003
L3         736 L2 NOT PY>2003

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4         385 DUP REM L3 (351 DUPLICATES REMOVED)

=> s l4 not simdax
L5         370 L4 NOT SIMDAX

=> s l4 and (renal or kidney)
L6          15 L4 AND (RENAL OR KIDNEY)

=> d l6 ibib abs 1-15

L6   ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:         2001:906809  CAPLUS
DOCUMENT NUMBER:          137:72913
TITLE:                    Effects of levosimendan, a novel inotropic
                          calcium-sensitizing drug, in experimental septic shock
```

AUTHOR(S): Oldner, Anders; Konrad, David; Weitzberg, Eddie; Rudehill, Anders; Rossi, Patrik; Wanecek, Michael
CORPORATE SOURCE: Department of Surgical Sciences, Section of Anaesthesiology and Intensive Care Medicine, Karolinska Institute, Stockholm, Swed.
SOURCE: Critical Care Medicine (2001), 29(11), 2185-2193 CODEN: CCMDC7; ISSN: 0090-3493
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Levosimendan is a novel inodilator that improves cardiac contractility by sensitizing troponin C to calcium. This drug has proved to be effective in treating advanced congestive heart failure but has not been evaluated in septic settings. The purpose of the present study was to study the effects of this drug in a porcine model of endotoxemia in a prospective exptl. study. All animals (fourteen land-race pigs) were anesthetized and catheterized for measurement of central and pulmonary hemodynamics. Ultrasonic flow probes were placed around the renal artery and portal vein to measure blood flow. A tonometer was placed in the ileum to measure mucosal pH. Levosimendan was given to six animals as a bolus (200 μg·kg-1) followed by a continuous infusion (200 μg·kg-1-hr-1). Thirty minutes after onset of levosimendan treatment, all animals received endotoxin (20 μg·kg-1-hr-1 for 3 h). At baseline, levosimendan induced a systemic vasodilation with a reduction in blood pressure and an increase in heart rate. A tendency to an increase in cardiac index did not reach statistical significance (p = .055). Cardiac index and systemic oxygen delivery were markedly improved in the levosimendan group during endotoxemia. Systemic vascular resistance and blood pressure were reduced in the levosimendan group. The latter parameter, however, was only different from the control group during the initial phase of endotoxin shock but not at the late, most pronounced phase of shock. Levosimendan also efficiently attenuated endotoxin-induced pulmonary hypertension. Portal venous blood flow and gut oxygen delivery were improved, but no concomitant reduction in endotoxin-induced intestinal mucosal acidosis was observed Renal blood flow was unaffected, as was the endotoxin-induced increase in plasma endothelin-1-like immunoreactivity. These findings support previous reports of calcium desensitization as a potential component in septic myocardial depression. Furthermore, the vasodilatory properties of this drug were well tolerated in the current model of hypodynamic endotoxin shock, and they may have contributed to improved regional blood flow as seen in the gut as well as improved systemic perfusion by means of reduced biventricular afterload. Pretreatment with levosimendan in pigs subjected to endotoxin shock improved cardiac output and systemic and gut oxygen delivery. In addition, pulmonary hypertension largely was attenuated without any adverse effects on gas exchange. These results are promising in several aspects, but the role of levosimendan in the treating circulatory failure in sepsis remains to be established.

OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (36 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1996:619297 CAPLUS
DOCUMENT NUMBER: 125:265511
ORIGINAL REFERENCE NO.: 125:49277a,49280a
TITLE: Influence of levosimendan, pimobendan, and milrinone on the regional distribution of cardiac output in anesthetized dogs
AUTHOR(S): Pagel, Paul S.; Hettrick, Douglas A.; Warltier, David

C.
CORPORATE SOURCE: Dep. Anesthesiol., Med. Coll. Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: British Journal of Pharmacology (1996), 119(3), 609-615
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The distribution of cardiac output during administration of levosimendan, a new myofilament calcium sensitizer, is unknown. The authors examined and compared the effects of levosimendan, pimobendan, and milrinone on regional tissue perfusion by use of the radioactive microsphere technique in barbiturate-anesthetized dogs. Hemodynamics and regional blood flow were determined before and during infusions of levosimendan (0.75, 1.5, and 3.0 μg kg-1 min-1), pimobendan (10, 20, and 40 μg kg-1 min-1), or milrinone (1.0, 2.0, and 4.0 μg kg-1 min-1). All three drugs caused similar increases in heart rate, cardiac output, and left ventricular + dP/dt and decreases in end-diastolic pressure and systemic vascular resistance. No changes in subendocardial, midmyocardial, and subepicardial blood flow occurred during administration of levosimendan. However, a redistribution of blood flow from subendocardium to subepicardium was observed Pimobendan increased midmyocardial. and subepicardial blood flow and reduced the endo/epi ratio to a greater degree than levosimendan. Milrinone did not affect myocardial perfusion. Levosimendan increased blood flow to the renal medulla and decreased renal medullary and cortical vascular resistance. Levosimendan increased blood flow to the small intestine and liver and reduced vascular resistance in these organs. Pimobendan increased hepatic blood flow to a greater degree than levosimendan but did not alter small intestinal perfusion. All three drugs decreased splenic blood flow to similar degrees. Levosimendan and pimobendan reduced cerebral vascular resistance. Levosimendan and milrinone reduced skeletal muscle vascular resistance. The results indicate that levosimendan, pimobendan, and milrinone cause subtlety different alterations in regional tissue perfusion while producing similar hemodynamics effects.
OS.CITING REF COUNT: 34 THERE ARE 34 CAPLUS RECORDS THAT CITE THIS RECORD (34 CITINGS)

L6 ANSWER 3 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1999087642 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9872607
TITLE: Parenteral inotropic support for advanced congestive heart failure.
AUTHOR: Leier C V; Binkley P F
CORPORATE SOURCE: Division of Cardiology, The Ohio State University, College of Medicine and Public Health, Columbus, OH 43210, USA.
SOURCE: Progress in cardiovascular diseases, (1998 Nov-Dec) Vol. 41, No. 3, pp. 207-24. Ref: 111
Journal code: 0376442. ISSN: 0033-0620. L-ISSN: 0033-0620.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 7 Jan 1999
AB Parenterally administered positive inotropic agents remain an important

component of the therapeutics of cardiac dysfunction and failure. Dobutamine, a catechol, remains the prototype of this drug group, but recently has been joined by the phosphodiesterase III inhibitor, milrinone. Compared with dobutamine, milrinone has greater vasodilating-unloading properties. The catecholamine, dopamine, is often used as a parenteral positive inotrope; but at moderate to high dose, it evokes considerable systemic vasoconstriction. At lower doses, dopamine appears to augment renal function. Levosimendan and toborinone, new compounds with several mechanisms of action, are under active clinical investigation and review for approval. Parenteral positive inotropic therapy is indicated for short-term (hours to days) treatment of cardiovascular decompensation secondary to ventricular systolic dysfunction, low-output heart failure. More prolonged or continuous infusion of one of these agents may be necessary as a "pharmacologic bridge" to cardiac transplantation, another definitive intervention, or more advanced, intense medical therapy. An occasional patient will require a continuous infusion via indwelling venous catheter and portable pump, simply to be able to be discharged from the hospital setting and function in the home environment. Intermittent parenteral inotropic therapy for chronic heart failure has provoked considerable controversy and passion among cardiologists and heart failure specialists; an attempt is made to present this topic in an objective manner.

L6 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35535 BIOSIS
DOCUMENT NUMBER: PREV200400033329
TITLE: Prognostic markers of levosimendan treatment efficacy in severe congestive heart failure: A prospective multicentre Study.
AUTHOR(S): Bocchi, E. [Reprint Author]; Guimaraes, G. [Reprint Author]; Vilas-Boas, F.
CORPORATE SOURCE: Medical School, Heart Institute (InCor), University of Sao Paulo, Sao Paulo, Brazil
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L6 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35534 BIOSIS
DOCUMENT NUMBER: PREV200400033328
TITLE: Levosimendan is efficacious in acute heart failure independent of renal function.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author]; Providencia, L. A. [Reprint Author]
CORPORATE SOURCE: Cardiology Dept., Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.

ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L6 ANSWER 6 OF 15 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:35533 BIOSIS
DOCUMENT NUMBER: PREV200400033327
TITLE: Levosimendan is beneficial in diabetics with acute heart failure.
AUTHOR(S): Franco, F. [Reprint Author]; Goncalves, F. [Reprint Author]; Castro, G. [Reprint Author]; Morais, M. Emilia [Reprint Author]; Andrade, C. [Reprint Author]; Goncalves, L. [Reprint Author]; Freitas, M. [Reprint Author]; Providencia, L. [Reprint Author]
CORPORATE SOURCE: Cardiology Department, Coimbra, Portugal
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 407. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004

L6 ANSWER 7 OF 15 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:15784 BIOSIS
DOCUMENT NUMBER: PREV200400013587
TITLE: Development of a comprehensive new endpoint for the evaluation of new treatments for acute decompensated heart failure: Results with levosimendan in the REVIVE-1 Study.
AUTHOR(S): Packer, M. [Reprint Author]; Colucci, W. S.; Fisher, L.; Massie, B. M.; Teerlink, J. R.; Young, J. B.; Garratt, C.
CORPORATE SOURCE: Medicine, Columbia University, New York, NY, USA
SOURCE: European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 24. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

L6 ANSWER 8 OF 15 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:47358 BIOSIS
DOCUMENT NUMBER: PREV199698619493
TITLE: The effects of renal failure on the pharmacokinetics of levosimendan.
AUTHOR(S): Sandell, E. P.; Antila, S.; Koisinen, H.; Pentikainen, P. J.
CORPORATE SOURCE: Orion Farmos, Cardiovascular Projects, Orionintie 1,

	FIN-02700 Espoo, Finland
SOURCE:	Therapie (Paris), (1995) Vol. 0, No. SUPPL., pp. 495. Meeting Info.: 1st Congress of the European Association for Clinical Pharmacology and Therapeutics. Paris, France. September 27-30, 1995. CODEN: THERAP. ISSN: 0040-5957.
DOCUMENT TYPE:	Conference; (Meeting) Conference; Abstract; (Meeting Abstract) Conference; (Meeting Poster)
LANGUAGE:	English
ENTRY DATE:	Entered STN: 2 Feb 1996 Last Updated on STN: 2 Feb 1996

L6 ANSWER 9 OF 15 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:	2003494488 EMBASE
TITLE:	Clinical decision making in managing the 'difficult' patient with chronic heart failure: Who, when, how, where?.
AUTHOR:	Krum, Henry, Prof. (correspondence)
CORPORATE SOURCE:	Dept. of Epidemiol. and Prev. Med., Monash Univ. Ctrl. and E. Clin. Sch., Alfred Hospital, Melbourne, Vic. 3004, Australia.
SOURCE:	European Heart Journal, Supplement, (Dec 2003) Vol. 5, No. I, pp. I88-I96. Refs: 58 ISSN: 1520-765X CODEN: EHJSFT
COUNTRY:	United Kingdom
DOCUMENT TYPE:	Journal; Conference Article; (Conference paper)
FILE SEGMENT:	018 Cardiovascular Diseases and Cardiovascular Surgery 030 Clinical and Experimental Pharmacology 037 Drug Literature Index 038 Adverse Reactions Titles
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 30 Dec 2003 Last Updated on STN: 30 Dec 2003

AB Chronic heart failure (CHF) is a complex disorder, and all patients with this condition could therefore be considered 'difficult'. Nevertheless, there are certain subgroups in whom management poses greater challenges. These include patients with advanced disease severity, complications arising from CHF, comorbidities, and patients in whom it is difficult to optimize standard therapies. Advanced disease is associated with reduced quality of life, frequent hospitalization and poor survival. Major challenges in advanced CHF include ensuring adequate tolerability of therapy, keeping patients out of hospital and decision making regarding palliation. Complications such as tachyarrhythmias and bradyarrhythmias may also alter management. CHF is a pro-thromboembolic state, but the role of anticoagulation and antiplatelet therapy is unclear. Weight loss is an independent prognostic marker for poor survival in complicated CHF, and therapies directed at reducing weight loss may improve outcome. Comorbid conditions that may affect decision making in the patient with CHF include aetiological contributors (e.g. ischaemic heart disease, hypertension, diabetes mellitus and anaemia) and other comorbid disorders such as respiratory disease, cognitive dysfunction, depression, renal failure and arthritis. In some clinical scenarios, optimal therapy may not easily be achieved. In patients with low systemic blood pressure, vasodilating drugs may be difficult to use. Bradyarrhythmias or bronchial hyperreactivity may limit the use of beta-blockers. Drug therapy may also be difficult to optimize in patients with advanced renal dysfunction. .COPYRGT. 2003 The European Society of Cardiology. Published by Elsevier Science Ltd.

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ACCESSION NUMBER: 2003301348 EMBASE
TITLE: Clinical use of inotropic therapy for heart failure: Looking backward or forward? Part I: Inotropic infusions during hospitalization.
AUTHOR: Stevenson, Lynne Warner, Dr. (correspondence)
CORPORATE SOURCE: Division of Cardiology, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115, United States.
SOURCE: Circulation, (22 Jul 2003) Vol. 108, No. 3, pp. 367-372. Refs: 50
ISSN: 0009-7322 CODEN: CIRCAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Aug 2003
Last Updated on STN: 14 Aug 2003

L6 ANSWER 11 OF 15 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003256920 EMBASE
TITLE: Gateways to clinical trials: May 2003.
AUTHOR: Bayes, M. (correspondence)
CORPORATE SOURCE: Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
AUTHOR: Rabasseda, X.; Prous, J.R.
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (May 2003) Vol. 25, No. 4, pp. 317-340. Refs: 143
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2003
Last Updated on STN: 17 Jul 2003

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity®, the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: 2F5, 2G12, Abetimus sodium, ABI-007, adalimumab, adefovir dipivoxil, AE-941, alefacept, altropane, aminolevulinic acid hydrochloride, aminolevulinic acid methyl ester, aminopterin, anakinra, aprinocarsen sodium, atazanavir, atlizumab, atomoxetine hydrochloride; B7-1 vaccine, bevacizumab, biricodar dicitrate, BMS-188667, brasofensine sulfate, bryostatin 1; Cantuzumab mertansine, CHS-828, cinacalcet hydrochloride, cipamfylline, creatine, CVT-3146; Darbepoetin alfa, DITPA, drotrecogin alfa (activated), duloxetine hydrochloride; Edatrexate, efalizumab, ENMD-0997, epoetin, erlosamide, esomeprazole magnesium, etiprednol dicloacetate, etoricoxib, everolimus, ezetimibe; Fampridine, fenretinide, FTY-720; IGF-I/IGFBP-3 IL-1 cytokine trap, ilodecakin, interferon beta, ISIS-104838, ISIS-2503, ISIS-5132, ivabradine hydrochloride; Lafutidine, lanthanum carbonate, L-Arginine hydrochloride, LEA29Y, lerdelimumab, levetiracetam, levobupivacaine hydrochloride,

levosimendan, lopinavir; Melagatran, mibefradil hydrochloride, miglustat, morphine-6-glucuronide; Nesiritide; Omalizumab, omapatrilat; p24-VLP, parecoxib sodium, peginterferon alfa-2a, peginterferon alfa-2b, pegsunercept, pitavastatin calcium, plevitrexed, prasterone, pregabalin, PRO-2000, prucalopride; Rapacuronium bromide, rebimastat, RGA-0853, rubitecan, ruboxistaurin mesilate hydrate, RWJ-67657; S-16020-2, sarizotan, SLV-306, stiripentol; TA-CIN, tenecteplase, teriparatide, tezacitabine, tipifarnib, trabectedin, troglitazone; Valdecoxib, vardenafil; Z-338, ziconotide. .COPYRGT. 2003 Prous Science. All rights reserved.

L6 ANSWER 12 OF 15 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003158036 EMBASE
TITLE: [Cardiac failure in intensive care].
Srdecni selhani v intenzivni peci.
AUTHOR: Parizkova, R., Dr. (correspondence)
CORPORATE SOURCE: Univerzita Karlova v Praze, Lekarska Fakulta v Hradci Kralove, Fakultni Nemocnice Hradec Kralove, 500 05 Hradec Kralove, Czech Republic.
AUTHOR: Parizkova, R., Dr. (correspondence)
CORPORATE SOURCE: Klin. Anesteziol. Resuscitace/I. M., Fakultni Nemocnice, 500 05 Hradec Kralove, Czech Republic.
SOURCE: Anesteziologie a Neodkladna Pece, (2003) Vol. 14, No. 2, pp. 103-110.
Refs: 27
ISSN: 0862-4968 CODEN: ANPEFF
COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
024 Anesthesiology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Czech
SUMMARY LANGUAGE: English; Czech
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 1 May 2003

AB Heart failure represents almost 5 % of all hospital admissions and both mortality and health care cost on account of those patients are high. The proportion of patients on ICU with heart failure of various origin (mostly as a results either of primary heart damage or as a result of secondary heart damage due to multiple organ failure) has increased rapidly during the last two decades. Heart failure occurs mostly as a result of ischaemic heart disease and the prevalence of heart failure increases in those with both ischaemic heart disease and hypertension. Increased sympathetic activity, renin-angiotensin-aldosterone axis, vasopressin, endothelin and atrial natriuretic peptides play the most important role in developing heart failure. Current definitions, diagnosis and recommended treatment of heart failure are based on recommendation issued by European Society of Cardiology. Echocardiography together with assessment of atrial natriuretic peptide plasma levels are preferred methods for diagnosis. The current therapeutic approach to heart failure is stratified according to levels of evidence based medicine methodology. The control of underlying cause and optimizing of myocardial oxygen delivery to failing heart without increasing oxygen consumption at the same time represent the cornerstone of therapy in heart failure patients. Diuretics, vasodilators together with inotropic agents (dobutamine, phosphodiesterase inhibitors and recently calcium sensitizers, if necessary), are the most recommended drugs in this setting. ACE inhibitors and beta-blockers are the key agents for long-term pharmacological therapy in chronic heart failure patients.

Non-pharmacological modalities are also mentioned.

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ACCESSION NUMBER: 2003156768 EMBASE
TITLE: Projecting future drug expenditures - 2003.
AUTHOR: Shah, Nilay D.; Vermeulen, Lee C. (correspondence)
CORPORATE SOURCE: Center for Drug Policy, Univ. of Wisconsin Hosp. and Clinics, 600 Highland Avenue, Madison, WI 53792, United States.
AUTHOR: Shah, Nilay D.
CORPORATE SOURCE: Dept. of Population Health Sciences, School of Medicine, Univ. Wisconsin-Madison (UW-Madison), Madison, WI, United States.
AUTHOR: Hoffman, James M.
CORPORATE SOURCE: Outcomes Res./Medication Use Policy, UWHC, Madison, WI, United States.
AUTHOR: Vermeulen, Lee C. (correspondence)
CORPORATE SOURCE: School of Pharmacy, UW-Madison, Madison, WI, United States.
AUTHOR: Hunkler, Robert J.; Hontz, Karrie M.
CORPORATE SOURCE: Business Development, IMS HEALTH, Plymouth Meeting, PA, United States.
SOURCE: American Journal of Health-System Pharmacy, (15 Jan 2003) Vol. 60, No. 2, pp. 137-149.
Refs: 46
ISSN: 1079-2082 CODEN: AHSPEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2003
Last Updated on STN: 1 May 2003

AB Drug expenditure projections for 2003 and factors likely to influence drug costs are discussed. The United States continues to face the challenge of increased growth in health expenditures, and drug expenditures are continuing to increase faster than the growth in total health care expenditures. These increases can be largely attributed to an increase in the average age of the U.S. population and technological advancement. On the basis of price inflation and non-price inflationary factors, including increases in volume, shifts in patient and therapeutic intensity, and expected approval of new drugs, a 10-12% increase in drug expenditures in 2003 for the inpatient setting and a 13.5-15.5% increase for ambulatory care settings are forecasted. While few new drugs are expected to greatly influence expenditures in 2003, the continued diffusion of recently approved drugs such as drotrecogin alfa and nesiritide will have a dramatic impact on total drug expenditures and must be carefully considered in the budgeting process. An agent likely to have a significant impact on HIV treatment is enfuvirtide, the first in a new class of antiretrovirals (fusion inhibitors), but its high cost ($10,000-$15,000 per year) may limit patients' access to this medication. An expanded user's guide is provided to assist the reader in appropriate application of this information in the drug budgeting process. Technological, demographic, and market-based changes and changes in public policy will continue to influence pharmaceutical expenditures in the coming year. An understanding of the overall drivers of medication expenditures and vigilance in monitoring pharmaceutical innovation are critical in the effective management of these resources.

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reserved on STN
ACCESSION NUMBER: 2003075961 EMBASE
TITLE: 15th Annual Congress of the European Society of Intensive Care Medicine, 29 September-2 October 2002, Barcelona, Spain: Clinical research to improve outcome.
AUTHOR: Dubois, Marc-Jacques (correspondence); Bouali, Redouane
CORPORATE SOURCE: Critical Care Medicine Division, University of Montreal Hospital, Montreal, Que., Canada. marc-jacques.dubois@umontreal.ca
AUTHOR: Verdant, Colin L.
CORPORATE SOURCE: Faculty of Medicine, University of Montreal, Montreal, Que., Canada.
SOURCE: Critical Care, (Feb 2003) Vol. 7, No. 1, pp. 91-94.
Refs: 12
ISSN: 1364-8535 CODEN: CRCAFM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
018 Cardiovascular Diseases and Cardiovascular Surgery
024 Anesthesiology
028 Urology and Nephrology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Feb 2003
Last Updated on STN: 27 Feb 2003

L6 ANSWER 15 OF 15 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002164027 EMBASE
TITLE: New therapeutic options in congestive heart failure: Part I.
AUTHOR: McMurray, John, Dr. (correspondence); Pfeffer, Marc A.
CORPORATE SOURCE: Clin. Res. Initiative Heart Failure, University of Glasgow, Wolfson Building, Glasgow G12 8QQ, United Kingdom.
SOURCE: Circulation, (30 Apr 2002) Vol. 105, No. 17, pp. 2099-2106.
Refs: 72
ISSN: 0009-7322 CODEN: CIRCAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002

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